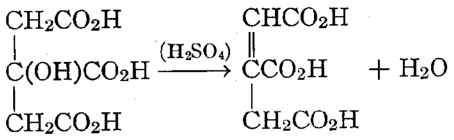
ORGANIC SYNTHESES

I

ACONITIC ACID



Submitted by William F. Bruce.
Checked by L. F. Fieser and C. H. Fisher.

1. Procedure

In a 1-l. round-bottomed flask equipped with a reflux condenser (Note 1) are placed 210 g. (1 mole) of powdered citric acid monohydrate and a solution of 210 g. (115 cc., 2 moles) of concentrated sulfuric acid in 105 cc. of water. The mixture is heated in an oil bath kept at a temperature of 140–145° for seven hours. The light brown solution is poured into a shallow dish, and the flask is rinsed with 10 cc. of hot glacial acetic acid. The liquid is allowed to cool slowly to 41–42° (Note 2), with occasional stirring to break up the solid mass of aconitic acid which separates, and the solid is collected on a suction funnel (Note 3). The material is pressed and drained thoroughly until practically dry, when it is removed and stirred to a homogeneous paste with 70 cc. of concentrated hydrochloric acid, cooled in an ice bath. The solid is collected on a suction funnel (Note 3), washed with two 10-cc. portions of cold glacial acetic acid, sucked thoroughly, and spread out in a thin layer on porous plate or paper for final drying (Note 4). This product contains practically no sulfate and is pure enough for most purposes. It is colorless, and when dry weighs 71–77 g. (41–44 per cent of the theoretical amount)

(Note 5). The point of decomposition determined under controlled conditions (Note 6) varies from 180° to 200°.

For purification the acid is crystallized from about 150 cc. of glacial acetic acid, using an acid-resistant filter for the hot solution (Note 7). Aconitic acid separates as small, colorless needles weighing 50–60 g., and about 10 g. more can be secured by concentrating the mother liquor under reduced pressure to one-third of its volume. The material is dried in the air and then in a desiccator containing sodium hydroxide in order to remove all traces of acetic acid. One crystallization usually is sufficient to bring the point of decomposition to 198–199° (Note 6).

2. Notes

1. A ground-glass connection is highly desirable.

2. By filtering at this point rather than at a lower temperature a separation from a small amount of low-melting material is accomplished without much loss of aconitic acid.

3. This material may be filtered conveniently by means of a sintered glass funnel, or by using a pad of pure wool flannel in an 8-cm. Büchner funnel.

4. In humid weather the solid often deliquesces, and this necessitates drying in a desiccator. The material retains acetic acid very tenaciously, and drying should be continued until the odor of the solvent no longer can be noticed.

5. A determination by the method of Pucher, Vickery, and Leavenworth [1] showed that 26 g. of citric acid remained in the sulfuric acid solution. It is inadvisable to use this solution for another run; the accumulation of water and by-products reduces considerably the yield and the quality of the product.

6. When heated in a capillary tube aconitic acid decomposes rather suddenly with vigorous gas evolution at a temperature which is highly dependent upon the rate of heating and the temperature at which the sample is introduced. In the literature [2] "melting points" ranging from 182.5° to 194.5° are recorded. The uncrystallized aconitic acid, when introduced at 180° into a small bath provided with mechanical agitation and heated at the rate of 2–3° per minute, usually decomposed at 189–190°. The once recrystallized material, introduced at 190°, decomposed at 198–199°; introduced at 195°, it decomposed at 204–205°. A determination on the Dennis bar,[3] the most reliable method for this type of compound, showed a decomposition point of 209°. The sample must be thoroughly dry to obtain the highest figures.

7. The hot solution is very destructive to filter paper. A convenient filter is made by preparing a 1–2 mm. mat of asbestos in a 6-cm. Büchner funnel, dusting onto this a 2–3 mm. layer of Norite, washing by suction, and heating the unit, together with a suction flask, in an oven at 120°. When dry and hot, the apparatus is ready for use.

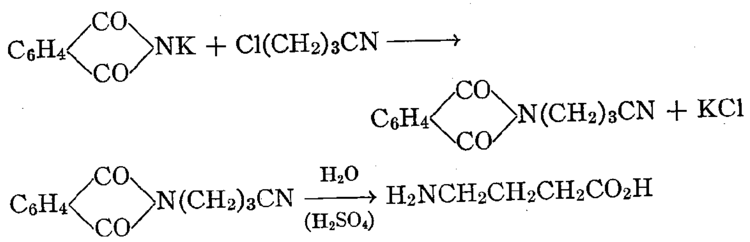
3. Methods of Preparation

Aconitic acid has been prepared from citric acid by the action of sulfuric acid [4] or hydrogen chloride,[5] or by heating.[6] It has been prepared also from methyl acetylcitrate [7] and from acetylcitric anhydride.[8] The method described is essentially that of Hentschel.[4] Phosphoric acid (85 per cent) can be used in place of sulfuric acid, but much closer regulation of the conditions seems necessary and the yield is not greatly improved.

[1] Pucher, Vickery, and Leavenworth, Ind. Eng. Chem., Anal. Ed. **6**, 190 (1934).
[2] Malachowski and Maslowski, Ber. **61**, 2521 (1928).
[3] Dennis and Shelton, J. Am. Chem. Soc. **52**, 3128 (1930).
[4] Hentschel, J. prakt. Chem. [2] **35**, 205 (1887).
[5] Hunäus, Ber. **9**, 1751 (1876).
[6] Pawolleck, Ann. **178**, 153 (1875).
[7] Anschütz and Klingemann, Ber. **18**, 1953 (1885).
[8] Easterfield and Sell, J. Chem. Soc. **61**, 1007 (1892).

II

γ-AMINOBUTYRIC ACID



Submitted by C. C. DeWitt.
Checked by W. W. Hartman and A. J. Schwaderer.

1. Procedure

In a 1-l. round-bottomed flask fitted with a tightly fitting cork stopper carrying an air condenser are placed 100 g. (0.54 mole) of finely powdered potassium phthalimide (Org. Syn. Coll. Vol. I, 114) and 52 g. (0.5 mole) of γ-chlorobutyronitrile (Org. Syn. Coll. Vol. I, 150). The flask is heated in an oil bath maintained at 150–180° for one and one-half hours (Note 1) and then allowed to cool. The excess potassium phthalimide and the potassium chloride formed are removed by extraction with several portions of boiling distilled water until the wash water gives no test for chloride ion. The flask is then cooled and the product caused to solidify, and the remaining water is decanted as completely as possible. The solid is treated with 140 cc. of concentrated sulfuric acid, and the mixture is warmed gently in an oil bath under a reflux condenser until all the γ-phthalimidobutyronitrile is brought into solution. Through the reflux condenser 200 cc. of distilled water is added carefully and the solution is refluxed vigorously for three hours. The mixture is cooled and allowed to stand overnight, and the phthalic acid is filtered off. The filtrate is transferred to a large evaporating dish, 1 l. of distilled water is added, and then an excess of barium

carbonate (about 550 g.) is added in small portions (Note 2). The mixture is evaporated nearly to dryness on the steam bath and the residue is stirred thoroughly with 1 l. of distilled water and again evaporated (Note 3). Finally 1 l. of distilled water is stirred with the solid and the mixture is filtered on a large Büchner funnel. The precipitate is washed with three 200-cc. portions of hot distilled water, and the filtrate and washings are concentrated to a volume of 200 cc. on the steam bath. After adding 2 g. of activated carbon the solution is filtered by suction, using a No. 42 Whatman paper, and the charcoal is washed with several small portions of hot distilled water. The filtrate is concentrated on the steam bath to the point of crystallization (about 75 cc.) and 375–500 cc. of absolute alcohol is added to precipitate the amino acid. The mixture is stirred well so that the yellow impurities are retained in the solvent and, after cooling, the colorless, crystalline product is collected and washed with absolute alcohol.

The alcoholic filtrate is evaporated to 50 cc., and 50 g. of barium hydroxide and 150 cc. of distilled water are added (Note 4). The mixture is refluxed for two hours and the excess barium hydroxide is precipitated with carbon dioxide. The barium carbonate is removed by filtration and washed with hot distilled water. A slight excess of sulfuric acid is added to the filtrate to liberate the amino acid from its barium salt, and an excess of barium carbonate is added to remove sulfate ion. The mixture is digested on the steam bath until effervescence ceases, and it is then filtered and the precipitate is washed with hot distilled water. The filtrate and washings are concentrated on the steam bath to a volume of 100 cc., decolorized with 1 g. of active carbon, filtered, and concentrated to the point of crystallization (about 25 cc.). The amino acid is precipitated by the addition of 150 cc. of absolute alcohol and the product is collected and washed with absolute alcohol.

The combined yield is 24–32 g. (47–63 per cent on the basis of the γ-chlorobutyronitrile used). The amino acid may be recrystallized by dissolving it in the least possible amount of distilled water and adding 5 to 7 volumes of absolute alcohol.

2. Notes

1. It is advisable to interrupt the heating after about forty-five minutes and thoroughly mix the pasty material by means of a glass rod. Longer heating of the reaction mass, although unnecessary, does no harm.

2. The reagent neutralizes the sulfuric acid and decomposes the ammonium sulfate, but it does not react with the amino acid.

3. The ammonia usually is removed completely by these two treatments, but if this is not the case the thorough mixing of the solid with water and the subsequent evaporation must be repeated.

4. The alcoholic filtrate contains appreciable amounts of pyrrolidone. The treatment with excess barium hydroxide converts this into the barium salt of the amino acid.[1,2]

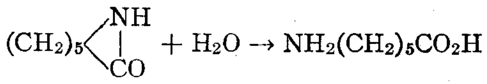
3. Methods of Preparation

γ-Aminobutyric acid has been prepared by the electrolytic reduction of succinimide to pyrrolidone and hydrolysis of the latter by means of barium hydroxide,[1] by the oxidation of piperylurethan with fuming nitric acid and the treatment of the resulting product with concentrated hydrochloric acid in sealed tubes at 100°,[3] and by the hydrolysis of the condensation product from *N*-(β-bromoethyl)-phthalimide and sodiomalonic ester.[4] The present method is a slight modification of that of Gabriel.[2]

[1] Tafel and Stern, Ber. **33**, 2224 (1900).
[2] Gabriel, ibid. **22**, 3335 (1889); **23**, 1771 (1890).
[3] Schotten, ibid. **16**, 643 (1883).
[4] Aschan, ibid. **24**, 2450 (1891).

III

ϵ-AMINOCAPROIC ACID



Submitted by J. C. Eck.
Checked by L. F. Fieser and C. H. Fisher.

1. Procedure

In a 500-cc. round-bottomed flask, 50 g. (0.442 mole) of 2-ketohexamethylenimine (p. 60) is added to a solution of 45 cc. of concentrated hydrochloric acid (sp. gr. 1.19) in 150 cc. of water. The solution is boiled for about one hour until it becomes clear (Note 1) and evaporated to dryness under reduced pressure on a steam bath.

The resulting ϵ-aminocaproic acid hydrochloride is treated in a manner similar to that used in the preparation of *dl*-alanine (Org. Syn. Coll. Vol. **1**, 20). The hydrochloride is dissolved in 1 l. of water in a 1.5-l. beaker and treated successively with 50 g. of powdered litharge, 25 g. of powdered litharge, 5 g. of freshly precipitated lead hydroxide, 25 g. of powdered silver oxide (Note 2), and finally hydrogen sulfide. During this procedure, the original volume is maintained by the addition of small amounts of water.

After the complete removal of halogen and metallic ions, the solution is concentrated to a volume of about 100 cc., and 300 cc. of absolute alcohol is added. Then the amino acid is precipitated by slowly adding 500 cc. of ether with stirring and cooling.

The resulting ϵ-aminocaproic acid is collected on a suction filter and dried in a desiccator. The yield of ϵ-aminocaproic acid melting at 201–203° is 52.5–53.5 g. (90–92 per cent of the theoretical amount).

2. Notes

1. This indicates that the hydrolysis is complete.

2. The exact amount of silver oxide required may be determined by titrating a sample of the solution with silver nitrate by the Volhard method.

3. Methods of Preparation

ε-Aminocaproic acid has been prepared by the hydrolysis of ε-benzoylaminocapronitrile,[1] by the hydrolysis of ethyl δ-phthalimidobutylmalonate,[2] and from cyclohexanoneoxime by rearrangement and hydrolysis.[3]

[1] von Braun and A. Steindorff, Ber. **38**, 176 (1905); von Braun, ibid. **40**, 1839 (1907); Ruzicka and Hugoson, Helv. Chim Acta **4**, 479 (1921); Marvel, MacCorquodale, Kendall, and Lazier, J. Am. Chem. Soc. **46**, 2838 (1924).

[2] Gabriel and Maass, Ber. **32**, 1266 (1899).

[3] Wallach, Ann. **312**, 188 (1900); Eck and Marvel, J. Biol. Chem. **106**, 387 (1934).

IV

1,2-AMINONAPHTHOL HYDROCHLORIDE AND 1,4-AMINONAPHTHOL HYDROCHLORIDE

$$C_{10}H_7OH + {}^+N_2C_6H_4SO_3^- + NaOH \rightarrow C_{10}H_6(OH)N{=}NC_6H_4SO_3Na + H_2O$$

$$C_{10}H_6(OH)N{=}NC_6H_4SO_3Na + 2\ Na_2S_2O_4 + 4\ H_2O \rightarrow C_{10}H_6(OH)NH_2 + 4\ NaHSO_3 + H_2NC_6H_4SO_3Na$$

Submitted by Louis F. Fieser.
Checked by C. R. Noller and W. R. White.

(*A*) *Diazotization of Sulfanilic Acid.*—A mixture of 105 g. (0.5 mole) of sulfanilic acid dihydrate, 26.5 g. (0.25 mole) of anhydrous sodium carbonate, and 500 cc. of water is heated and stirred until all the sulfanilic acid has dissolved, and the solution is then cooled in an ice bath to 15° (sodium sulfanilate begins to crystallize at this temperature). A solution of 37 g. (0.54 mole) of sodium nitrite in 100 cc. of water is added and the resulting solution is poured at once onto a mixture of 106 cc. (1.25 moles) (Note 1) of concentrated hydrochloric acid (sp. gr. 1.18) and 600 g. of ice contained in a 2-l. beaker. The solution, from which *p*-benzenediazonium sulfonate separates on stirring, is allowed to stand in an ice bath for fifteen to twenty-five minutes, during which time the naphtholate solution is prepared.

(*B*) *Coupling: Orange II.*—Seventy-two grams of β-naphthol (0.5 mole) is dissolved in the warm solution obtained by dissolving 110 g. (2.75 moles) (Note 2) of sodium hydroxide in 600 cc. of water in a 5-l. flask, and the solution is cooled to about 5° by the addition of 400 g. of ice. The suspension of the diazonium salt then is added and the mixture is stirred well and allowed to stand without external cooling for one hour (Note 3). The azo compound soon separates from the red solution and eventually forms a stiff paste.

(*B'*) *Coupling: Orange I.*—The procedure is the same as in (*B*) except that the alkaline solution of α-naphthol (Note 4) is cooled to 25° before adding the ice (Note 5). The azo dye in this case does not crystallize but forms a deep purple-red solution.

(*C*) *Reduction: 1,2-Aminonaphthol Hydrochloride.*—The suspension of Orange II is heated to 45–50°, when all the material dissolves with slight evolution of gas. About one-tenth of 230 g. (about 1.1 moles) of technical sodium hydrosulfite (Note 6) is added cautiously and the mixture is stirred until the froth subsides; the remainder is then added without delay. The yellow material which first separates (probably the hydrazo compound) soon is converted into the nearly colorless aminonaphthol. In order to complete the reduction and to give an easily filterable product the mixture is heated strongly until it begins to froth; it is then cooled to 25° by stirring in an ice bath, and the pink or cream-colored product is collected and washed free from the slightly yellow mother liquor with water.

The crude aminonaphthol is washed into a beaker containing a solution at 30° of 2 g. of stannous chloride (dihydrate) and 53 cc. (0.63 mole) of concentrated hydrochloric acid in 1 l. of water. On stirring the mixture the amine soon dissolves, leaving in suspension a small amount of fluffy material which is easily distinguishable from the original lumps (Note 7). The solution is clarified by stirring (without heating) for five minutes with 10 g. of decolorizing carbon, and it is then filtered by suction. The pale yellow solution is treated with 50 cc. of concentrated hydrochloric acid and heated to the boiling point, a second 50 cc. of the acid being added as the heating progresses. The color becomes somewhat fainter during this process. The vessel containing the hot solution is transferred to an ice bath and allowed to cool undisturbed, and the 1-amino-2-naphthol hydrochloride soon separates in the form of large, perfectly colorless needles. When fairly cold, 100 cc. of concentrated hydrochloric acid is added and the solution is cooled to 0° before collecting the product (Note 8). The hydrochloride is washed with a cold solution of 50 cc. of concentrated hydrochloric acid in 200 cc. of water and dried on a filter paper at a temperature not above 30–35°. The yield

is 70–83 g. (72–85 per cent of the theoretical amount). The material will remain colorless, or very nearly so, if protected from the light in storage. The fresh solution in water is only faintly colored and leaves but a trace of residue on filtration.

Although this material is suitable for most purposes, it may be purified further in the following manner. It is dissolved by heating in a solution of 2 g. of stannous chloride and 2 cc. of concentrated hydrochloric acid in 1 l. of water, and the hot solution is clarified by filtration through a 5-mm. mat of decolorizing carbon (Note 9). The yellow or red color which may develop disappears on reheating to the boiling point. After the addition of 100 cc. of concentrated hydrochloric acid the solution is allowed to cool in an ice bath, treated with a second 100 cc. of acid, cooled to 0°, and collected and washed as before. The crystalline product is colorless, ash-free, and of analytical purity. The loss in the crystallization of an 80-g. lot amounts to 5–10 g. (6–12 per cent).

(*C'*) *Reduction: 1,4-Aminonaphthol Hydrochloride.*—Since this isomer is more sensitive to air oxidation than the ortho compound and since the solubility of its hydrochloride is greater, some slight modifications of the procedure given in (*C*) are advisable. The reduction proceeds well and the tan suspension of the aminonaphthol need be heated only to about 70° to effect a sufficient coagulation. The mixture is cooled quickly with constant stirring to prevent undue oxidation, and the product is washed with a fresh 1 per cent solution of sodium hydrosulfite rather than with water. A solution of 2 g. of stannous chloride and 63 cc. of hydrochloric acid in 800 cc. of water (at 30°) is used to dissolve the crude amine, and the transference to this solution should be made with dispatch. Even after thorough stirring it is usually necessary to apply heat in order to dissolve all the particles of the amine. The solution is filtered directly by suction, without treatment with charcoal. It usually acquires a rather deep red color. One hundred cubic centimeters of concentrated hydrochloric acid is added, the solution is heated to the boiling point for five to ten minutes, and a second 100-cc. portion of the acid is added. During this heating the color fades to a light yellow,

and on cooling to 0° a mass of small, nearly colorless crystals is obtained.

This material (dry weight, 77–80 g.) (Note 10), without being dried, is crystallized from 700 cc. of water containing 2 g. of stannous chloride and 2 cc. of concentrated hydrochloric acid, following exactly in all other respects the procedure given above at the end of Section (*C*). The 1,4-aminonaphthol hydrochloride forms small, nearly colorless needles of a high degree of purity. The solution in water is faintly pink, and the crystals may acquire a slight pink color after a few weeks. The yield is 70–73 g. (72–75 per cent of the theoretical amount).

2. Notes

1. Diazotization can be accomplished by the use of just one equivalent of acid (0.5 mole), but the solution of the diazoic acid, $NaO_3SC_6H_4N{=}NOH$, so formed is much less stable than the suspension of the inner salt which results from the use of more acid.

2. The excess alkali is not required for the process of coupling, but rather to provide conditions suitable for the reduction.

3. The yield is not improved by allowing a longer period for the reaction. Under the conditions specified, the mixture during the coupling remains at a temperature of 5–10°.

4. The α-naphthol should be free from the β-isomer; if the material is very highly colored it is advisable to purify it by distillation at atmospheric pressure. Material melting at 95–96° is satisfactory.

5. A low temperature is required during the coupling in order to avoid the formation of the disazo compound.

6. If the hydrosulfite is of poor quality more will be needed, in which case an additional amount of sodium hydroxide should also be added.

7. The solution is highly supersaturated, but it will remain so unless allowed to stand for an undue amount of time. It is also a mistake to add the quantity of concentrated hydrochloric acid specified to a suspension of the aminonaphthol, for this may initiate crystallization.

8. An alternate method of crystallization is to add all the hydrochloric acid (200 cc.) to the boiling solution and to allow this to cool slowly; very large, thick needles result. In the presence of stannous chloride there is no danger of a darkening of the solution as the result of oxidation.

9. This method is preferable to the usual one when dealing with a substance sensitive to air oxidation.

10. The material is slightly yellow and may redden on drying; it probably contains a trace of 2,4-diamino-1-naphthol.

3. Methods of Preparation

1-Amino-2-naphthol has been obtained from β-naphthylamine [1] and, more practically, from β-naphthol through the nitroso compound or an azo compound. Nitroso-β-naphthol has been reduced in alkaline solution with hydrogen sulfide [2,3] or sodium hydrosulfite,[4] but early workers encountered difficulty in converting the amine into its hydrochloride without undue oxidation. Sulfur dioxide was employed as an antioxidant but it is wholly inadequate. Reduction in an acidic medium, usually with stannous chloride, has been more satisfactory. The isolation of the amine stannochloride and its tedious decomposition with hydrogen sulfide [5] are unnecessary, for the amine hydrochloride can be caused to crystallize essentially free from tin by avoiding an excess of the reducing agent.[2,6,7] Nitroso-β-naphthol has been reduced also with zinc dust and sulfuric acid,[8] but the quality of the material, used for conversion to the quinone, is in some doubt.

The nitroso derivative has disadvantages as an intermediate in that this involves handling either a voluminous precipitate or a large volume of solution, and in that some tar is likely to form; hence an azo compound is preferable. Technical Orange II has been reduced in a neutral or alkaline medium with sodium sulfide[2] or sodium hydrosulfite,[9] the sulfanilic acid being eliminated as the soluble sodium salt. With stannous chloride, the necessity of isolating the amine stannochloride [1] can be avoided by using just the calculated amount of reagent, the resulting mixture of amine hydrochloride and sulfanilic acid being sepa-

rated with an alkaline buffer.[2] Witt [10] found that the sulfanilic acid can be kept in solution if this is sufficiently acidic, and with this improvement Russig [11] worked out a procedure for the preparation and reduction of Orange II which was reported to give excellent yields but which, judging from the results of conversion to the quinone, affords a poor product. In the experience of the present author the method is uncertain and usually unsatisfactory.

Orange II also has been reduced with zinc dust and hydrochloric acid,[12] by electrolysis,[13] and by catalytic hydrogenation.[14]

The only practical method of preparing 1,4-aminonaphthol is from α-naphthol through an azo dye, the nitroso compound [5] not being readily available. The majority of investigators have reduced technical Orange I with stannous chloride [1,11,15,16,17,18] by the procedures discussed above, and benzeneazo-α-naphthol has been reduced by the same reagent.[5,19] In order to make possible the use of crude, technical α-naphthol a method has been developed [20] for the preparation of the benzeneazo compound, its separation from the isomeric dye coming from the β-naphthol present as well as from any disazo compound by extraction with alkali, and the reduction of the azo compound in alkaline solution with sodium hydrosulfite. The process, however, is tedious and yields an impure product.

The present method [21] is applicable with slight modifications to the preparation of both the ortho and para aminonaphthols and to many homologues, benzologues, and heterocyclic isologues of these substances. The chief feature of novelty is in the use of stannous chloride as an antioxidant in preparing and crystallizing the amine hydrochlorides.

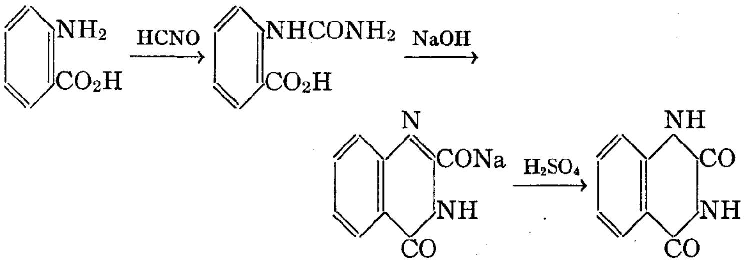
1 Liebermann and Jacobson, Ann. **211**, 49 (1882).
2 Groves, J. Chem. Soc. **45**, 294 (1884); Stenhouse and Groves, Ann. **189**, 153 (1877).
3 Lagodzinski and Hardine, Ber. **27**, 3075 (1894); Böeseken, Rec. trav. chim. **34**, 272 (1915); Porai-Koschitz, Ger. pat. 463,519 [Chem. Zentr. II, 1384 (1928)].
4 Conant and Corson, Org. Syn. **11**, 8 (1931).
5 Grandmougin and Michel, Ber. **25**, 974 (1892).
6 Zincke, Ann. **268**, 274 (1892).
7 Paul, Z. angew. Chem. **10**, 48 (1897).
8 Skita and Rohrmann, Ber. **63**, 1482 (1930).

9 Grandmougin, ibid. **39**, 3561 (1906).
10 Witt, ibid. **21**, 3472 (1888).
11 Russig, J. prakt. Chem. (2) **62**, 56 (1900); Böeseken, Rec. trav. chim. **41**, 780 (1922).
12 Zincke, Ann. **278**, 188 (1894).
13 Ger. pat. 121,835 [Chem. Zentr. II, 152 (1901)]; Hubbuch and Lowy, C. A. **23**, 343 (1929).
14 Ger. pat. 406,064 [Chem. Zentr. I, 1531 (1935)].
15 Liebermann, Ann. **183**, 247 (1876).
16 Liebermann, Ber. **14**, 1796 (1881).
17 Seidel, ibid. **25**, 423 (1892).
18 Zincke and Wiegand, Ann. **286**, 70 (1895).
19 Fuchs and Pirak, Ber. **59**, 2456 (1926).
20 Conant, Lutz and Corson, Org. Syn. Coll. Vol. **1**, 41 (1932).
21 L. F. Fieser and M. Fieser, J. Am. Chem. Soc. **57**, 491 (1935).

V

BENZOYLENE UREA

(2,4-Diketotetrahydroquinazoline)



Submitted by N. A. Lange and F. E. Schiebley.
Checked by W. W. Hartman and J. B. Dickey.

1. Procedure

In a 3-l. beaker a mixture of 20 g. (0.146 mole) of anthranilic acid, 700 cc. of warm water (35°), and 11 cc. (11.6 g., 0.19 mole) of glacial acetic acid is stirred mechanically and allowed to cool to room temperature. A freshly prepared solution of 15 g. (0.185 mole) of potassium cyanate (Note 1) in 50 cc. of water is then added dropwise with stirring over a period of fifteen to twenty minutes (Note 2). After stirring the resulting pasty mixture for twenty minutes, 200 g. (5 moles) of flaked sodium hydroxide (Note 3) is added slowly in small portions. The reaction mixture is kept below 40° by cooling in a cold-water bath. A clear solution is obtained momentarily, but in a short time a fine granular precipitate of the monosodium salt of benzoylene urea precipitates. After cooling the mixture overnight in an ice box the precipitated sodium salt is collected on a Büchner funnel, using a hardened filter paper (Note 4). The colorless salt is dissolved in 1 l. of hot water (90–95°), and the solution is filtered and heated to boiling in a 3-l. beaker. The benzoylene urea is

precipitated by adding dilute sulfuric acid (1 : 1) with vigorous stirring until the liquor is acid to litmus. The product separates as a hydrate (Note 5) which forms small, lustrous, colorless needles. The material is collected on a Büchner funnel, washed with 200 cc. of water, and dried in an oven at 100°. The yield is 19.5–20.5 g. (82.5–87 per cent of the theoretical amount).

2. Notes

1. The yield is highly dependent upon the quality of the potassium cyanate employed, and some samples were found worthless for the purpose. The yields given were realized using Eastman's regular grade of potassium cyanate.

2. If the addition is too rapid the odor of isocyanic acid (remindful of that of sulfur dioxide) becomes strong and the yield is diminished.

3. The commercial grade of flaked sodium hydroxide dissolves readily and is convenient to handle. Any silica present is not objectionable since it is removed by filtering the redissolved sodium salt before precipitating the product with acid.

4. Schleicher and Schüll's hardened filters (No. 575, 9 cm.) are satisfactory.

5. Benzoylene urea is reported to separate from aqueous solution with from one to five molecules of water of crystallization.

3. Methods of Preparation

Benzoylene urea has been prepared by passing cyanogen into a solution of anthranilic acid in alcohol and hydrolyzing the resulting 2-ethoxy-4-ketodihydroquinazoline,[1] by fusing anthranilic acid with urea,[2,3] and by the action of aqueous cyanic acid on anthranilic acid.[2,3,4,5] The procedure described is adapted from that of Bogert and Scatchard[5] with several modifications.

[1] Griess, Ber. **2**, 415 (1869).
[2] Griess, J. prakt. Chem. [2] **5**, 371 (1872).
[3] Bogert and Scatchard, J. Am. Chem. Soc. **41**, 2056 (1919).
[4] Gabriel and Colman, Ber. **38**, 3561 (1905); Scott and Cohen, J. Chem. Soc. **119**, 664 (1921).
[5] Bogert and Scatchard, J. Am. Chem. Soc. **38**, 1611 (1916).

VI

BROMAL

$(CH_3CHO)_3 + 9\ Br_2 \rightarrow 3\ CBr_3CHO + 9\ HBr$

Submitted by F. A. LONG and J. W. HOWARD.
Checked by W. W. HARTMAN and G. L. BOOMER.

1. Procedure

IN a 2-l. three-necked, round-bottomed flask fitted with a liquid-sealed mechanical stirrer, a dropping funnel, and an efficient reflux condenser are placed 720 g. (226 cc., 4.5 moles) of bromine (Note 1) and 1.5 g. of sulfur (Note 2). A glass tube is connected to the top of the condenser to carry the evolved hydrogen bromide to a gas trap (Org. Syn. 14, 2). Sixty-nine grams (69 cc., 0.52 mole) of dry paraldehyde (Note 1) is added slowly, with stirring, over a period of about four hours. The reaction proceeds under its own heat during the addition of the paraldehyde; subsequently the mixture is heated externally for two hours at 60–80°. The solution is distilled and a fraction collected over the range 155–175° (Note 3).

On redistillation under reduced pressure there is obtained 220–240 g. (52–57 per cent yield) of reddish-yellow bromal, boiling at 59–62°/9 mm., or 71–74°/18 mm.

2. Notes

1. The bromine is dried by shaking with concentrated sulfuric acid; the paraldehyde is dried over calcium chloride.

2. The use of sulfur as a catalyst increases the yield 5–10 per cent and causes no trouble in the purification.

3. The fore-run amounts to 90–180 g. and consists mostly of bromine, bromoacetaldehyde, and dibromoacetaldehyde. An additional quantity of bromal may be obtained by treating this

material with a small amount of bromine, heating for two hours at 60–80°, and distilling as before.

3. Methods of Preparation

Bromal has been prepared by brominating a solution of paraldehyde in ethyl acetate,[1] and by passing bromine vapor through absolute alcohol.[2]

[1] Pinner, Ann. **179**, 67 (1875).
[2] Schäffer, Ber. **4**, 366 (1871).

VII

p-BROMOBENZALDEHYDE

$$p\text{-}BrC_6H_4CH_3 + 2\ Br_2 \rightarrow p\text{-}BrC_6H_4CHBr_2 + 2\ HBr$$
$$p\text{-}BrC_6H_4CHBr_2 + H_2O \rightarrow p\text{-}BrC_6H_4CHO + 2\ HBr$$

Submitted by GEORGE H. COLEMAN and G. E. HONEYWELL.
Checked by W. W. HARTMAN and A. J. SCHWADERER.

1. Procedure

IN a 1-l. three-necked flask fitted with a mechanical stirrer, a reflux condenser, a thermometer, and a dropping funnel is placed 100 g. (0.58 mole) of *p*-bromotoluene (Org. Syn. Coll. Vol. 1, 131). The stem of the dropping funnel and the thermometer should reach nearly to the bottom of the flask. The upper end of the condenser is connected to a gas absorption trap (Org. Syn. **14**, 2). The flask is heated with stirring in an oil bath until the temperature of the liquid reaches 105°. The liquid is illuminated with an unfrosted 150-watt tungsten lamp, and 197 g. (61.8 cc., 1.23 moles) of bromine is added slowly from the separatory funnel (Note 1). About one-half of the bromine is added during the first hour, during which time the temperature is kept at 105–110°. The rest is added during about two hours, while the temperature is raised to 135°. When all the bromine has been added the temperature is raised slowly to 150°.

The crude product (Note 2) is transferred to a 2-l. flask and mixed thoroughly with 200 g. of powdered calcium carbonate. About 300 cc. of water is added and the mixture is heated cautiously (Note 3) and then refluxed for fifteen hours to effect hydrolysis. The product is then distilled in a rapid current of steam (Note 4), and the distillate is collected in 500-cc. portions, cooled, and the *p*-bromobenzaldehyde is collected and dried in a desiccator. From the first liter of distillate 50–60 g. of *p*-bromobenzaldehyde melting at 55–57° is obtained. An additional

15–20 g. of product melting at 50–56° is obtained in about 2 l. more of distillate (Note 5). This may be purified through the bisulfite addition compound (Note 6) and yields 13–18 g. of product melting at 55–57°. The total yield of pure aldehyde is 65–75 g. (60–69 per cent of the theoretical amount).

2. Notes

1. The rate of addition of the bromine should be so regulated that a large excess of unreacted bromine does not accumulate in the reaction mixture. The amount of bromine present may be roughly estimated by the color of the solution and by the amount of bromine vapor carried into the condenser.

2. *p*-Bromobenzal bromide is a lachrymator and also produces a burning sensation on the skin. Washing the affected parts with alcohol gives relief.

3. In order to avoid breaking the flask the mixture is heated first on a water bath and then on a wire gauze over a flame with continuous shaking until the liquid begins to boil. The refluxing may then be continued without danger.

4. The inlet tube for steam should reach to the bottom of the distillation flask. A 16-mm. bulb on the end of this tube with four 0.8-mm. openings helps to insure thorough mixing of the heavy residue. If this is not well stirred the aldehyde distils very slowly. It is well to connect the flask to the condenser through a large Hopkins still head in order to prevent the entrainment of foam during the distillation.

5. Five to ten grams of crude *p*-bromobenzoic acid can be obtained by acidifying the solution left in the distilling flask.

6. The material is triturated with saturated sodium bisulfite solution (2 cc. per gram), and after about three hours the pasty mixture is filtered with suction. The addition product is washed with absolute alcohol and then with ether and transferred to a flask fitted for steam distillation. Excess sodium carbonate solution is added and the aldehyde is distilled in a current of steam.

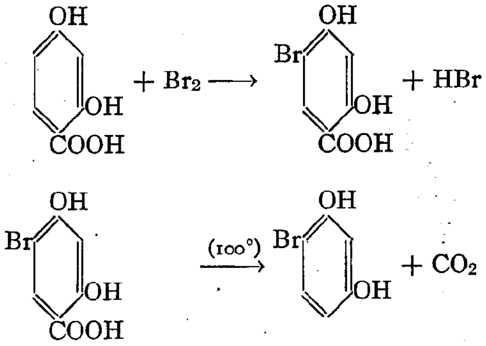
3. Methods of Preparation

p-Bromobenzaldehyde has been prepared by the oxidation of *p*-bromotoluene with chromyl chloride,[1] by saponification of the acetal from *p*-bromophenylmagnesium bromide and orthoformic ester,[2] by the oxidation of ethyl *p*-bromobenzyl ether with nitric acid,[3] by the oxidation of *p*-bromobenzyl bromide with lead nitrate,[4] and by the hydrolysis of *p*-bromobenzal bromide in the presence of calcium carbonate.[5]

1 Wörner, Ber. **29**, 153 (1896).
2 Tschitschibabin, ibid. **37**, 188 (1904); Bodroux, Bull. soc. chim. [3] **31**, 587 (1904); Gattermann, Ann. **393**, 223 (1912).
3 Errera, Gazz. chim. ital. **17**, 206 (1887).
4 Jackson and White, Ber. **11**, 1043 (1878); Am. Chem. J. **3**, 32 (1881).
5 Adams and Vollweiler, J. Am. Chem. Soc. **40**, 1738 (1918).

VIII

4-BROMORESORCINOL



Submitted by R. B. Sandin and R. A. McKee.
Checked by W. W. Hartman and J. B. Dickey.

1. Procedure

In a 1-l. flask fitted with a mechanical stirrer and a dropping funnel are placed 46.2 g. (0.3 mole) of 2,4-dihydroxybenzoic acid (β-resorcylic acid, Org. Syn. **10**, 94) and 350 cc. of glacial acetic acid. The stirrer is started and the mixture is warmed until solution results (45°) and allowed to cool to 35°. Through the dropping funnel is then added a solution of 48 g. (15 cc., 0.3 mole) of bromine in 240 cc. of glacial acetic acid with vigorous stirring over a period of about one hour. The temperature of the reaction mixture remains at 30–35° throughout the reaction. When all the bromine is added the solution is poured into 5 l. of water, and the mixture is cooled to 0–5° and allowed to stand for several hours. The fine, white crystals of 2,4-dihydroxy-5-bromobenzoic acid are collected on a 10-cm. Büchner funnel and washed with about 500 cc. of cold water. The crude product, after air drying at room temperature, melts at 194–200° and

weighs 55–60 g. For purification it is dissolved in 1500 cc. of boiling water, and the solution is refluxed for one hour (Note 1), filtered while hot, and cooled in an ice bath. The material which crystallizes is collected, washed with 100 cc. of cold water, and air dried. The yield of colorless 2,4-dihydroxy-5-bromobenzoic acid melting at 206.5–208.5° (corr.) is 40–44 g. (57–63 per cent of the theoretical amount).

Thirty grams of purified 2,4-dihydroxy-5-bromobenzoic acid is refluxed for twenty-four hours with 375 cc. of water, and the resulting solution is filtered, cooled, and extracted with a 400-cc. and a 200-cc. portion of ether. The ether is removed by evaporation, and the 4-bromoresorcinol is dried on a steam bath. The yield of product melting at 100–102° (Note 2) is 22–22.5 g. (90–92 per cent of the theoretical amount).

2. Notes

1. The 2,4-dihydroxy-3,5-dibromobenzoic acid invariably present is in this way converted into the very soluble 2,4-dibromoresorcinol and removed. The monobromo acid is decarboxylated much more slowly.

2. Some samples were obtained with melting points ranging from 77° to 93°, but on dissolving the samples in chloroform and evaporating the solvent the values rose to 100–102°. This is not believed to be a process of purification.

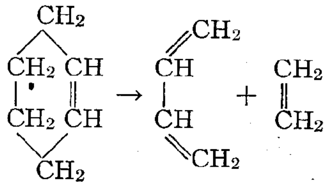
3. Methods of Preparation

4-Bromoresorcinol has been prepared by the monobromination of resorcinol monobenzoate and subsequent hydrolysis,[1] from 2-bromo-5-aminophenol by the diazo reaction,[2] by treating resorcinol with dichlorourea and potassium bromide,[3] and by the bromination of 2,4-dihydroxybenzoic acid followed by decarboxylation.[4] The above procedure is based particularly upon the observations of Rice.[4]

[1] Fries and Lindemann, Ann. **404**, 61 (1914).
[2] Fries and Saftien, Ber. **59**, 1254 (1926).
[3] Likhosherstov, J. Gen. Chem. (U.S.S.R.) **3**, 172 (1933) [C. A. **28**, 1676 (1934)].
[4] Zehenter, Monatsh. **2**, 480 (1881); **8**, 293 (1887); Van Hemmelmayr, ibid. **33**, 977 (1912); **34**, 374 (1913); Rice, J. Am. Chem. Soc. **48**, 3125 (1926); Davis and Harrington, ibid. **56**, 129 (1934).

IX

1,3-BUTADIENE



Submitted by E. B. Hershberg and John R. Ruhoff.
Checked by Wallace H. Carothers and J. Harmon.

1. Procedure

Cyclohexene (Note 1) is boiled in the flask B, shown in Fig. 1, and the vapor is passed over a cracking element consisting of an expansible grid threaded with resistance ribbon (L) (Notes 2 and 3). The boiling flask (B) is supported over a 250-watt bowl heater provided with a rheostat, and the current in the cracking element is taken from a 115-volt a-c. or d-c. source and controlled by a second rheostat of 10-ampere capacity (Note 4). In order to trap any cyclohexene which passes the coil condenser, the gas-delivery tube D is connected to a tube leading close to the bottom of a 500-cc. distilling flask immersed in an ice bath. The exit tube of the flask is connected with a short section of rubber tubing to a receiver for condensing the butadiene, consisting of a large test tube with the entrance tube leading half way to the bottom and an exit tube at the top for conducting the ethylene (saturated with butadiene) to a hood or outdoors. The receiver is cooled in a Dewar flask containing solid carbon dioxide and a eutectic mixture of equal parts by weight (or volume) of chloroform and carbon tetrachloride.

The flask B is two-thirds filled with cyclohexene, and, with the cooling water flowing, this is heated to vigorous boiling.

When the vapor has displaced the air from the apparatus *completely* (Note 5), the current is turned on in the cracking unit.

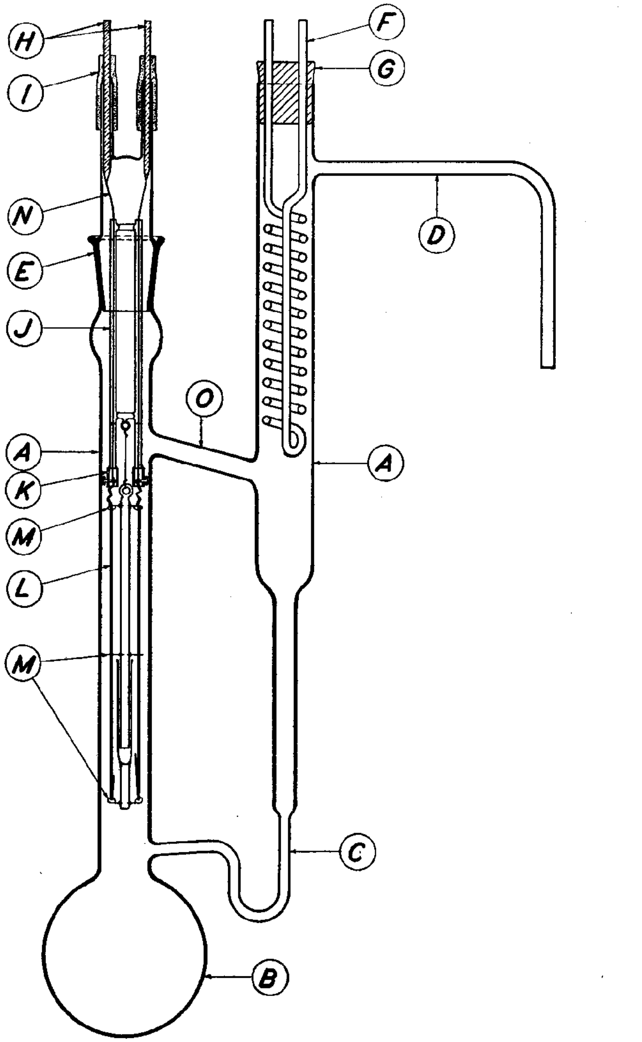


FIG. 1

By adjusting both the rate of boiling and the current the ribbon is maintained at a bright red heat over its entire length. Very

rapid refluxing is necessary in order to prevent undue carbonization on the filament and tar formation on the glass walls (Note 6). The generator can be run intermittently or until the charge is exhausted.

The butadiene collected is purified by a bulb-to-bulb distillation, the receiver in the cooling mixture being replaced by a similar container to which it is connected by means of rubber tubing and into which the butadiene is allowed to distil. The product is quite satisfactory for most uses, as in the Diels-Alder reaction (Note 7). The cracking element uses about 500 watts at 8.7 amperes and produces 25–30 g. of butadiene per hour. The yield, based on the cyclohexene consumed (Note 8) and on redistilled product, is 65–75 per cent of the theoretical amount. High-boiling residues accumulating in the boiling flask should be removed after preparing 100–150 g. of butadiene (Note 9).

2. Notes

1. In preparing cyclohexene by the dehydration of cyclohexanol with sulfuric acid (Org. Syn. Coll. Vol. 1, 177) the time can be shortened to about two hours by boiling the mixture in a round-bottomed flask provided with a reflux condenser with water maintained at about 75°.[1] A tube at the top leads to a downward cold-water condenser.

Cyclohexene can be prepared on a large scale still more rapidly and efficiently by the distillation of cyclohexanol over silica gel[2] or, better, activated alumina. Using a 25-mm. tube packed with 8- to 14-mesh activated alumina (Aluminum Company of America) and heated to 380–450° over a 30-cm. length, 1683 g. of cyclohexanol was dehydrated in about four hours. After separating the water, drying with sodium sulfate, and fractionating with a simple column, 1222 g. (89 per cent yield) of cyclohexene, b.p. 82–84°, was obtained.

2. *Apparatus.*—The unit shown in Fig. 1 is constructed of Pyrex glass, and the following is a summary of satisfactory dimensions for the various tubings (outer diameters) and of other specifications: A, 32-mm. tubing; B, 500-cc. flask; C, 7-mm. tubing; D, 8-mm. tubing; E, No. 35 standard taper

joint; F, coil of $\frac{3}{16}$-in. copper tubing (see Note 3); G, cork stopper; H, $\frac{1}{8}$-in. brass rod; I, rubber tubing; J, 3-mm. glass tubing; K, brass electrical connectors; L, Chromel C resistance ribbon No. 37 B. and S. gauge, 1.9–2 ohms per foot, width $\frac{1}{16}$ in., length 56 to 60 in. (see below); M, tungsten wire-loop supports sealed into the suspended glass rod; the center supports are of 0.01-in. (dia.) wire, those at the top and bottom of 0.015-in. (dia.) wire; N, copper wire No. 22 B. and S. gauge; O, 12-mm. tubing.

The ribbon L of the cracking element is threaded between the tungsten loops M, of which there are five each at the top and bottom and eight at the center. The unit is suspended with a copper wire from the glass cross-support as shown. The lower end is free to drop down as the resistance wire expands; this prevents short-circuiting of the element.

The composition of the filament is of importance in determining the yield and the performance of the apparatus. With nickel-chromium alloys excessive carbonization occurs and the yield is poor. Much better results are obtained with the nickel-iron-chromium alloys called Chromel C and Nichrome Alloy Wire.

3. To provide for the proper functioning of the coil condenser even in warm weather it is advisable to increase the number of turns to 30–40, although the condenser as shown is satisfactory with tap water at 4–10°.

4. A slide-wire rheostat of 2-ampere capacity wound on a hollow enameled iron tube will carry the required current if a stream of cooling water is passed through the tube.

5. An explosion may occur if the filament is heated while an appreciable amount of air is still present. Furthermore, the heating element will burn out at once if an adequate supply of cyclohexene vapor is not supplied, since the current passing through the wire is far above the normal rating for air.

6. In case of excessive carbonization the rate of boiling should be increased or the filament temperature slightly lowered. In general the vapor velocity should be as high as possible without exceeding the capacity of the copper condenser.

7. The crude product contains appreciable amounts of C_2, C_3, and C_6 fractions. The actual butadiene content lies between 82 and 88 per cent. If very pure material is desired the butadiene is converted into the tetrabromide and this is crystallized and reconverted to the hydrocarbon by means of zinc and alcohol.[3]

8. The cyclohexene collecting in the ice trap ordinarily is returned to the boiling flask; in determining the percentage conversion this was combined with any material left in the boiler and the pure starting material present recovered by fractionation.

9. The apparatus may be used also for the preparation of ketene from acetone (Org. Syn. Coll. Vol. 1, 324).

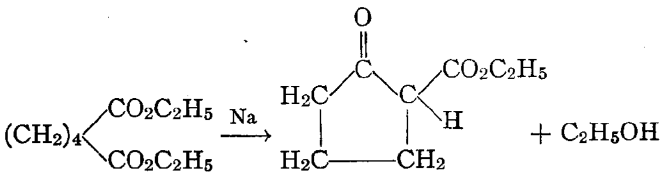
3. Methods of Preparation

The numerous methods for the preparation of gaseous products containing more or less butadiene are reviewed to 1919 by Beilstein.[4] More recently a laboratory preparation of the hydrocarbon starting with butyl chloride has been described,[5] and Jacobson [6] has modified the Harries [7] method utilizing 2,3-dibromobutene, and also has reported the preparation of crude butadiene by passing crotyl chloride over soda lime at 530–550°. The pyrolysis of cyclohexene to butadiene, originally disclosed in the patent literature,[8] is the only method definitely demonstrated to yield directly a product consisting essentially of butadiene.[3,9] The principle of the method is the same as in Harries' preparation of isoprene by cracking dipentene.[10]

[1] Kistiakowsky, Ruhoff, Smith and Vaughan, J. Am. Chem. Soc. **58**, 140 (1936).
[2] Bartlett and Berry, ibid. **56**, 2684 (1934).
[3] Kistiakowsky, Ruhoff, Smith, and Vaughan, ibid. **58**, 146 (1936).
[4] Beilstein, "Handbuch der organischen Chemie," 4th ed., Vol. I, pp. 249–250; Spl. Vol. I, pp. 107–109.
[5] Muskat and Northrup, J. Am. Chem. Soc. **52**, 4043 (1930).
[6] Jacobson, ibid. **54**, 1545 (1932).
[7] Harries, Ann. **383**, 176 (1911).
[8] Ger. pat. 252,499 [Chem. Zentr. II, 1708 (1912)].
[9] Zelinskiĭ, Mikhaĭlov, and Arbuzov, J. Gen. Chem. (U.S.S.R.) **4**, 856 (1934) [C. A. **29**, 2152 (1935)].
[10] Harries and Gottlob, Ann. **383**, 228 (1911).

X

2-CARBETHOXYCYCLOPENTANONE



Submitted by P. S. PINKNEY.
Checked by L. F. FIESER and T. L. JACOBS.

1. Procedure

A 3-l. three-necked, round-bottomed flask is fitted with a mercury-sealed mechanical stirrer (Note 1), a 250-cc. dropping funnel, and a reflux condenser protected from the air by means of a calcium chloride tube. In the flask are placed 23 g. (1 gram atom) of sodium and 250 cc. of dry toluene (Note 2). The stirrer is started, and 202 g. (1 mole) of ethyl adipate (Note 3) is added from the dropping funnel at such a rate that the addition is complete in about two hours. The reaction usually starts immediately on addition of the ethyl adipate. The temperature of the oil bath is maintained at 100–115° during the addition and for about five hours longer. Dry toluene is added through the condenser from time to time in order to keep the reaction mixture fluid enough for efficient stirring (Note 4). Between 750 cc. and 1000 cc. of toluene is added in this manner.

The reaction mixture is cooled in an ice bath and slowly poured into 1000 cc. of 10 per cent acetic acid cooled to 0° (ice-salt mixture). The toluene layer is separated, washed once with water, twice with cooled 7 per cent sodium carbonate solution, and again with water. The toluene is removed by distillation at ordinary pressure, and the residue is distilled under reduced

pressure. The yield is 115–127 g. (74–81 per cent of the theoretical amount) of a product boiling at 83–88°/5 mm. or 79–84°/3 mm. (Note 5).

2. Notes

1. The Hershberg [1] stirrer, shown in part in Fig. 2, provides very efficient agitation of this or other pasty mixture. Two glass rings are sealed to the end of a stirrer shaft at right angles to one another, and each is threaded with B. and S. No. 18

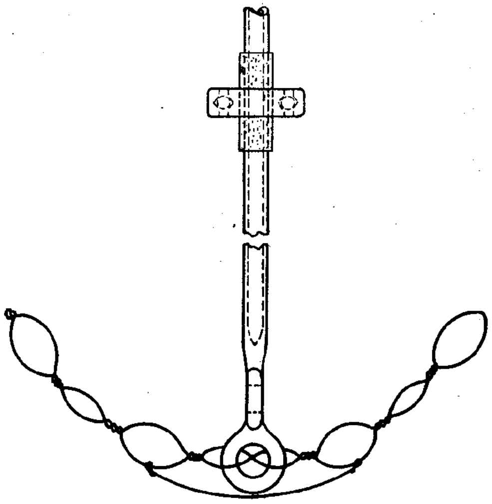


FIG. 2

Chromel or Nichrome wire (in the drawing the wire is shown only for the lower ring; the upper wire is not provided with a cross brace). The stirrer is easily introduced and removed through a narrow opening and in operation it follows the contour of the flask. It is convenient to use glass tubing for the stirrer shaft and to provide this with a pair of small ball bearings slipped on over short sections of rubber tubing (one of these bearings is shown in the drawing).

The yields reported were obtained using this stirrer; with various other stirrers it was seldom possible to duplicate the results.

2. The toluene is dried by distillation from sodium.

3. Ethyl adipate is easily prepared[2] by refluxing 175 g. (1.2 moles) of adipic acid, 175 g. (222 cc.) of ethyl alcohol, 450 cc. of ordinary benzene, and 80 g. (43.5 cc.) of concentrated sulfuric acid for five hours on the steam bath. The yield of ester boiling at 136–137°/19 mm. is 218 g. (90 per cent of the theoretical amount).

4. If the reaction mixture is allowed to become too thick for efficient stirring, or if the temperature of the oil bath is raised above 115–120°, the solid sodium derivative will cake on the sides of the flask. This makes the complete removal of the reaction mixture from the flask and the decomposition of the sodium derivative more difficult.

5. According to the literature,[3,4] the product obtained in this manner may contain ethyl adipate. To remove this, the product is cooled to 0° and run slowly into 600 cc. of 10 per cent potassium hydroxide solution maintained at 0° with ice-salt. Water is added until the salt which separates has dissolved, and the cold alkaline solution is extracted twice with 200-cc. portions of ether. The alkaline solution, kept at 0°, is run slowly into 900 cc. of 10 per cent acetic acid solution with stirring, the temperature remaining below 1° (ice-salt). The oil which separates is taken up in 400 cc. of ether, and the aqueous solution is extracted with four 250-cc. portions of ether. The ether extract is washed twice with cold 7 per cent sodium carbonate solution and dried over sodium sulfate. After removal of the ether the residue is distilled, b.p. 79–81°/3 mm. The recovery is only 80–85 per cent, and in a well-conducted preparation the ethyl adipate eliminated amounts to less than one per cent of the total product. Unless the preparation has proceeded poorly the tedious purification ordinarily is best omitted.

If material free from all traces of ethyl adipate is desired, time and material can be saved by omitting the first distillation (observation of the checkers). The toluene solution of the crude 2-carbethoxycyclopentanone is cooled to 0° and added slowly with stirring to 300 cc. of 10 per cent potassium hydroxide solution maintained below 1°. Cold water is added until the slightly soluble potassium salt has dissolved. The toluene layer is then separated and washed twice with 150-cc. portions of cold, 10 per cent potassium hydroxide solution. After each washing, cold water is added to dissolve any solid which separates. The toluene solution, now very light yellow in color, is finally washed twice with 150-cc. portions of cold water. The aqueous solutions are combined, extracted with 250 cc. of ether, and treated as described for the alkaline solution above. The yield is 100–115 g. (64–74 per cent).

3. Methods of Preparation

2-Carbethoxycyclopentanone has been prepared from ethyl adipate by the action of sodium,[2,3,4] sodamide,[5] and sodium ethylate.[6] The method in the above procedure is based upon the work of Cornubert and Borrel.[3]

[1] Hershberg, Ind. Eng. Chem. Anal. Ed. **8**, 313 (1936).

[2] van Rysselberge, Bull. acad. roy. Belg. (Sci.) [5] **12**, 171 (1926) [Chem. Zentr. II, 1846 (1926)].

[3] Cornubert and Borrel, Bull. soc. chim. [4] **47**, 301 (1930).

[4] Bouveault, ibid. [3] **21**, 1019 (1899); Zelinsky and Ouchakoff, ibid. [4] **35**, 484 (1924).

[5] Bouveault and Locquin, ibid. [4] **3**, 440 (1908).

[6] Wislicenus and Schwanhäusser, Ann. **297**, 112 (1897).

XI

CELLOBIOSE

$$C_{12}H_{14}O_{11}(COCH_3)_8 + 8\ CH_3OH \xrightarrow{(CH_3ONa)} C_{12}H_{22}O_{11} + 8\ CH_3COOCH_3$$

Submitted by GÉZA BRAUN.
Checked by REYNOLD C. FUSON, WILLIAM E. ROSS, and WILLIAM P. CAMPBELL.

1. Procedure

IN a 500-cc. three-necked flask, provided with a mercury-sealed stirrer and a calcium chloride tube, 68 g. (0.1 mole) of α-cellobiose octaacetate, m.p. 220–222° (p. 36), is suspended in 300 cc. of methyl alcohol (absolute). A solution, prepared by dissolving 0.25 g. (0.01 gram atom) of sodium in 50 cc. of methyl alcohol, is added and the mixture is stirred vigorously for one hour at room temperature (Note 1). The mixture becomes thin as the hydrolysis proceeds and the solvent acquires a slight color. After the time specified the crystalline solid is collected by suction filtration, washed with four 25-cc. portions of methyl alcohol, and dried at 40°. The weight of the nearly colorless crude cellobiose corresponds closely to the theoretical amount (34 g.). For purification it is dissolved in 125 cc. of hot water containing a few drops of glacial acetic acid and the solution is clarified with 1–2 g. of Norite and filtered by suction. The colorless filtrate is concentrated under reduced pressure to a small volume, continuing until a large portion of the cellobiose has crystallized, and the crystalline magma is washed into an Erlenmeyer flask with 100 cc. of methyl alcohol. The mixture is stirred well and allowed to stand for several hours for completion of the crystallization, and the sugar is collected on a Büchner funnel, washed with 25 cc. of methyl alcohol, and dried at 40°. The yield of pure cellobiose, $[\alpha]_D^{20°}$ + 34.8° (in 6 per cent aqueous

solution), is 31 g. (91 per cent of the theoretical amount). On concentrating the mother liquor to a small volume and adding alcohol as before, 1 g. of equally pure product is obtained, making the total yield 94 per cent of the theoretical amount (Note 2).

2. Notes

1. The reaction may be carried out equally satisfactorily by shaking the mixture mechanically in a stoppered bottle.

2. Using an earlier procedure,[1] in which a solution of the octaacetate in chloroform is treated with sodium methylate solution and then with water, the yields of pure cellobiose amounted to 67–79 per cent of the theoretical quantity.

3. Methods of Preparation

Cellobiose was prepared first by Skraup and König [2] by the saponification of the octaacetate with alcoholic potassium hydroxide, and the method was improved by Pringsheim and Merkatz.[3] Aqueous barium hydroxide also has been employed [4] for the purpose, and methyl alcoholic ammonia has been used extensively for the hydrolysis of carbohydrate acetates. The method of catalytic hydrolysis with a small quantity of sodium methylate was introduced by Zemplén,[1] who considered the action to be due to the addition of the reagent to the ester-carbonyl groups of the sugar acetate and the decomposition of the addition compound by reaction with alcohol.[5] The present procedure, reported by Zemplén, Gerecs, and Hadácsy,[6] is a considerable improvement over the original method [1] (see Note 2).

[1] Zemplén, Ber. **59**, 1254 (1926).
[2] Skraup and König, ibid. **34**, 1115 (1901).
[3] Pringsheim and Merkatz, Z. physiol. Chem. **105**, 173 (1919).
[4] Abderhalden and Zemplén, ibid. **72**, 58 (1911).
[5] Zemplén and Kunz, Ber. **56**, 1705 (1923).
[6] Zemplén, Gerecs, and Hadácsy, ibid. **69**, 1827 (1936).

XII

α-CELLOBIOSE OCTAACETATE

$$(C_{12}H_{20}O_{10})_n + n\,H_2O + 8n\,(CH_3CO)_2O \rightarrow n\,C_{12}H_{14}O_{11}(COCH_3)_8 + 8n\,CH_3CO_2H$$

Submitted by GÉZA BRAUN.
Checked by REYNOLD C. FUSON, WILLIAM E. ROSS and WILLIAM P. CAMPBELL.

1. Procedure

IN a 1-l. wide-mouth bottle with a glass stopper 400 cc. of acetic anhydride is cooled to −10° in a freezing mixture and 36 cc. of concentrated sulfuric acid is added at once with constant stirring. The temperature of the solution rises to about 20°. The bottle is removed from the freezing mixture and 20 g. of absorbent cotton (Note 1) is worked into the liquor immediately with a heavy glass rod. While stirring constantly, the bottle is warmed in a water bath maintained at 60° until the temperature of the mixture reaches 45° (about ten minutes), and then it is removed and the temperature is kept from rising above 55° by suitable cooling with running water, stirring being continued throughout (Note 2). After about twenty minutes (total) the mixture becomes thin, and at this point it is cooled to 50° and a second 20-g. portion of cotton is added with stirring, again keeping the temperature from rising above 55°. The process of cooling to 50° and adding 20 g. of cotton is repeated at intervals of about ten minutes until 100 g. of cotton in all has been introduced. After the final addition stirring is continued until the mixture becomes thin (about ten minutes) and the bottle is stoppered and heated in a bath maintained at 50° for one hour, during which time the cotton dissolves completely to a thin, light brown syrup. The stoppered container is then kept in an oven at 35° for seven days.

The solution darkens to a deep wine-red color, and α-cellobiose octaacetate begins to crystallize on the second day (Note 3). After seven days at 35° the semi-crystalline mass is stirred into 20 l. of cold water. With good stirring the flocculent precipitate of α-cellobiose octaacetate and cellulose-dextrin acetates soon becomes crystalline, and after standing for one to two hours the solid is collected on a 12.5-cm. Büchner funnel, washed free from acid with cold water, and drained thoroughly. The moist product, weighing about 250 g., is triturated with 250 cc. of warm methyl alcohol, and, after cooling to room temperature, the undissolved solid is collected on a 7-cm. Büchner funnel, washed with three 50-cc. portions of methyl alcohol, and dried at 40°. The yield of fairly pure α-cellobiose octaacetate is 69–74 g. For purification it is dissolved in 300 cc. of chloroform and the solution is filtered by suction into a dry receiver through a pad prepared by dusting Norite onto a Büchner funnel and washing this with alcohol. The chloroform solution is filtered while the pad is still wet with alcohol, and the filter is washed at once with 100 cc. of chloroform without interruption in the filtration. The colorless filtrate is concentrated at reduced pressure until the acetate begins to crystallize (about 250 cc.), the crystals are redissolved by warming, and the solution is poured into 750 cc. of warm methyl alcohol. The acetate begins to crystallize at once as small needles which eventually form a thick paste. The mixture is cooled to 0° with stirring, and after about one hour the material is collected, washed with 100 cc. of methyl alcohol, and dried at 40°. The yield of colorless α-cellobiose octaacetate, m.p. 220–222°, $[\alpha]_D^{20°}$ + 41.6°, is 65–69 g. (35–37 per cent of the theoretical amount, assuming that the cotton contains 10 per cent of moisture) (Notes 4, 5, and 6).

For further purification a solution of the material in 350 cc. of chloroform is clarified if necessary and poured into 750 cc. of methyl alcohol, and the mixture is cooled to 0°. The yield of the pure acetate, m.p. 225–226°, $[\alpha]_D^{20°}$ + 42.5°, is 61–65 g. The constants are not altered by further crystallizations.

2. Notes

1. Pure commercial cotton or filter paper may be used. These materials ordinarily contain 7–10 per cent of moisture.

2. Effective stirring and careful control of the reaction are essential for obtaining good yields. If left uncontrolled, the temperature may rise quickly above 100° with considerable decomposition.

3. The crystallization is accelerated by scratching the walls of the jar or by seeding. Seed is obtained easily by pouring a small portion of the reaction mixture into a large amount of water; the precipitate is separated, treated with alcohol, and dried at 40°.

4. In earlier experiments a temperature of 30–40° was maintained during the addition of the cotton (which then required more time), and the acetolysis was allowed to proceed at room temperature for six days. The yield of product melting at 220–222° was 50–56 g., but rose to 62–70 g. when the period of digestion was extended to eight days.

5. The quantities can be doubled without change in the procedure or the yield.

6. Pringsheim's method[1] of isolating the acetate gives equally good results. Instead of pouring the acetolysis mixture into water, it is kept at 0° for one to two days and the crystalline material is collected on a large Büchner funnel and washed with 50 cc. of ice-cold acetic anhydride. Cellulose-dextrin acetates and other by-products pass into the filtrate. The crude mass is digested with 200 cc. of warm methyl alcohol, collected, and crystallized from chloroform-alcohol as above. The yield is 65–68 g., m.p. 220–222°.

3. Methods of Preparation

The preparation of α-cellobiose octaacetate by the acetolysis of cellulose was discovered by Franchimont,[2] and the process has been studied carefully by a number of other investi-

gators.[1,3,4,5] The observations of Freudenberg[4] and Klein[5] were particularly useful in developing the present procedure.

[1] Pringsheim and Merkatz, Z. physiol. Chem. **105**, 173 (1919).

[2] Franchimont, Ber. **12**, 1941 (1879).

[3] Skraup and König, Monatsh. **22**, 1011 (1901); Maquenne and Godwin, Bull. soc. chim. (3) **31**, 854 (1904); Schliemann, Ann. **378**, 366 (1911); Ost, ibid. **398**, 338 (1913).

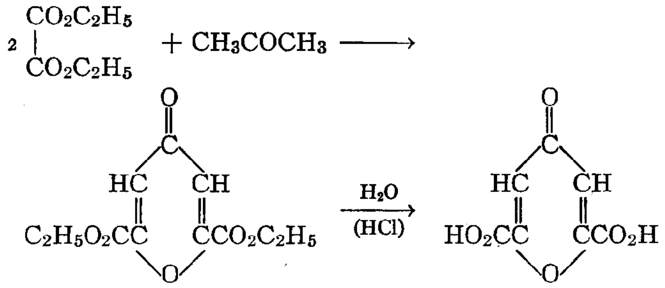
[4] Freudenberg, Ber. **54**, 767 (1921).

[5] Klein, Z. angew. Chem. **25**, 1409 (1912).

XIII

CHELIDONIC ACID

(γ-Pyrone-2,6-dicarboxylic Acid)



Submitted by E. Raymond Riegel and F. Zwilgmeyer.
Checked by Reynold C. Fuson and William E. Ross.

1. Procedure

In a 1-l. round-bottomed flask fitted with a reflux condenser protected by a calcium chloride tube 46 g. (2 gram atoms) of sodium is dissolved in 600 cc. of absolute alcohol (Note 1). About one hour is required for the addition of the sodium, and another hour for its complete solution. Toward the end of the reaction the flask may be heated with a small smoky flame. While the sodium is being dissolved, the following materials are weighed in dry, stoppered containers: 58 g. (1 mole) of dry acetone (Note 2), 150 g. (1.03 moles) of freshly distilled ethyl oxalate (Org. Syn. Coll. Vol. 1, 256), and 160 g. (1.1 moles) of ethyl oxalate.

About half of the sodium ethylate solution is poured into a 3-l. round-bottomed, three-necked flask provided with a liquid-sealed stirrer and a reflux condenser; the other half is kept warm by a small flame. The first half of the solution is allowed to

cool until a solid begins to appear and 58 g. of dry acetone mixed with 150 g. of ethyl oxalate is added at once and the stirrer is set in motion. Heat is evolved and the liquid turns brown, but remains clear. As soon as any turbidity appears, the other half of the hot sodium ethylate solution is poured into the mixture together with 160 g. of ethyl oxalate, the two streams being allowed to mix as they flow into the flask. The liquid initially is clear and of a deep brown color, but after stirring for about thirty minutes the mixture becomes practically solid. The flask is then connected with a condenser for distillation and heated in an oil bath at 110° until 150 cc. of alcohol has distilled. The flask is protected by a calcium chloride tube and the reaction mixture is cooled to 20°. The sodium derivative is removed to a 3-l. beaker by means of a glass rod and treated with a mixture of 300 cc. of concentrated hydrochloric acid (sp. gr., 1.19) and 800 g. of cracked ice (Note 3). All lumps are carefully crushed and the creamy yellow suspension of ethyl chelidonate is collected on a 15-cm. Büchner funnel. The ester is removed from the filter, stirred with about 100 cc. of ice water, and again collected (Note 4). For hydrolysis the crude material is heated with 300 cc. of concentrated hydrochloric acid in a 5-l. flask (Note 5) on the steam bath for twenty hours. After cooling to 20° the solid, hydrated acid is collected on a 10-cm. Büchner funnel, washed with two 50-cc. portions of ice water, and dried, first at 100° for two hours, and then at 160° to constant weight to remove the water of crystallization. The yield of product decomposing at 257° (corr.) is 140–145 g. (76–79 per cent of the theoretical amount).

2. Notes

1. A good grade of absolute alcohol should be used (Org. Syn. Coll. Vol. 1, 254).
2. The acetone is dried for several days over calcium chloride, filtered, and distilled.
3. The temperature must be kept as low as possible during the neutralization for any undue rise in temperature results in a darkening of the product.

4. The crude ester, after a further washing and after being dried in a vacuum desiccator over sulfuric acid, melts at 98–100° and weighs 220 g. (91 per cent of the theoretical amount).

5. A large flask is used because the mixture froths seriously at first. If the frothing becomes troublesome it may be stopped by adding a little ether.

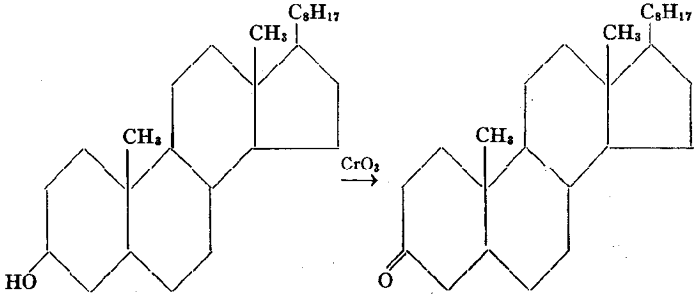
3. Methods of Preparation

Natural chelidonic acid is obtained from the herb celandine (*Chelidonium majus*). The synthesis from ethyl oxalate and acetone was first described by Claisen;[1] the process was simplified by Willstätter and Pummerer [2] and further improved by Ruzicka and Fornasir.[3] The present procedure is modelled after that of the last-mentioned investigators.

[1] Claisen, Ber. **24**, 111 (1891).
[2] Willstätter and Pummerer, ibid. **37**, 3744 (1904).
[3] Ruzicka and Fornasir, Helv. Chim. Acta **3**, 811 (1920).

XIV

CHOLESTANONE



Submitted by William F. Bruce.
Checked by L. F. Fieser and R. P. Jacobsen.

1. Procedure

A solution of 50 g. of dihydrocholesterol (0.13 mole) (Note 1) in 50 cc. of benzene is added slowly with cooling (Note 2) to a solution of 68 g. (0.23 mole) of crystalline sodium dichromate, 50 cc. of glacial acetic acid, and 90 cc. of concentrated sulfuric acid in 300 cc. of water in a 3-l. flask. The mixture is agitated thoroughly in a shaking device or by efficient stirring (Note 3) for six hours at 25–30° (Note 4).

The benzene solution is separated and washed twice with 100 cc. of water, once with 200 cc. of 5 per cent potassium hydroxide, and twice with water, and in case the solution is not colorless it is clarified with 1 g. of Norite. The benzene is removed by distillation and the resulting syrup is dissolved in 300 cc. of alcohol by heating. The solution on cooling deposits cholestanone as well-formed needles. The yield of collected, washed, and air-dried material, m.p. 129–130°, is 41.5–42 g. (83–84 per cent of the theoretical amount). The addition of 80 cc. of water to the filtrate gives about 2 g. of material melting at 125–126°.

2. Notes

1. Material melting at 140–141° (p. 45) is satisfactory. The presence of a trace of cholesterol is not objectionable since this is converted into acidic products which are removed in the course of the purification.

2. When the solutions are mixed without cooling the temperature rises to about 60° and the yield is somewhat less.

3. The checkers employed a Hershberg stirrer (p. 31).

4. The agitation may be continued for twice the period without appreciable difference in yield. Six hours is regarded as the minimum time for the quantity specified.

3. Method of Preparation

Cholestanone has been prepared by the oxidation of dihydrocholesterol with chromic anhydride in acetic acid solution.[1] The yield is sometimes diminished as a result of the partial acetylation of the sterol.

[1] Diels and Abderhalden, Ber. **39**, 884 (1906); Willstätter and Mayer, ibid. **41**, 2199 (1908); Vavon and Jacubowicz, Bull. soc. chim. [4] **53**, 584 (1933).

XV

DIHYDROCHOLESTEROL

(β-Cholestanol)

$$C_{27}H_{45}OH + H_2 \rightarrow C_{27}H_{47}OH$$

Submitted by (*A*) W. F. Bruce and (*B*) J. O. Ralls.
Checked by L. F. Fieser, R. P. Jacobsen, and M. S. Newman.

1. Procedure

(*A*) *From Cholesterol.*—One hundred grams (0.26 mole) of commercial cholesterol is crystallized from 250 cc. of glacial acetic acid, using 1 g. of Norite if required, and the purified material (Note 1) is transferred, conveniently without being dried, to a hydrogenation vessel equipped with a thermometer and a heating device (Note 2). Three hundred cubic centimeters of purified glacial acetic acid (Note 3) and 0.5 g. of platinum oxide are added, and the hydrogenation is conducted at 65–75° at a slight positive pressure. The total amount of hydrogen usually is absorbed in two to four hours (Note 4). After replacing the hydrogen by air the solution is filtered hot and the product is obtained by crystallization and concentration. The total yield of air-dried, partially acetylated dihydrocholesterol, m.p. 130–135°, is 85–90 g.

Unless a specially purified product (see below) is desired, the crude material is heated for three hours on the steam bath with 400 cc. of alcohol and a solution of 25 g. of sodium hydroxide in 100 cc. of water. After cooling, the product is collected, washed, and crystallized from 500 cc. of alcohol. The yield is 75–80 g. (75–80 per cent of the theoretical amount), and a well-dried sample (Note 5) melts at 140–141°.

(*B*) *From Cholesteryl Acetate* (Note 6).—Five grams of cholesteryl acetate (Note 7) and 0.1 g. of platinum oxide are

suspended in 25 cc. of absolute ether and 50 cc. of purified glacial acetic acid (Note 3), and the hydrogenation is conducted at room temperature at a slight positive pressure. The reaction is complete in ten to fifty minutes. The solution is filtered, using ether to dissolve any crystallized material, and after removing the solvent by distillation at reduced pressure the residue is either saponified as above or purified in the following manner.

Purification by the Method of Anderson and Nabenhauer.[1]—A solution of 20 g. of crude, partially or completely acetylated dihydrocholesterol in 200 cc. of carbon tetrachloride is placed in a separatory funnel and treated with 100 cc. of acetic anhydride. About 5 cc. of concentrated sulfuric acid is added dropwise through the stem of the inverted funnel with cooling and shaking until there is no further increase in color. A blue or green color develops, the intensity depending on the amount of cholesterol present in the sample. After fifteen to twenty minutes about 10 cc. of water is added by drops and with cooling and gentle shaking until two distinct layers form. The carbon tetrachloride solution (upper layer) is separated and washed free of acid with sodium chloride or sodium carbonate solution (pure water gives emulsions). After drying with sodium sulfate, the solvent is removed by distillation at diminished pressure and the residue is saponified as above with alcoholic alkali and crystallized from alcohol. The purified dihydrocholesterol weighs 12–14 g. and melts, after thorough drying (Note 5), at 142–143°. It gives a faint Liebermann-Burchard reaction (Note 8) only after ten to fifteen minutes.

2. Notes

1. The dry weight is 90–95 g. Some samples may require recrystallization.

2. See Org. Syn. Coll. Vol. 1, 54. Alternate arrangement: a round-bottomed, long-necked flask is supported at the top by a two-piece clamp with a loosened checknut, connected below to an eccentric, and heated in motion by means of a stationary microburner.

3. Glacial acetic acid is refluxed for one hour with 5 g. of potassium permanganate per liter and distilled.

4. The catalyst sometimes loses its activity when about half of the theoretical amount of hydrogen has been absorbed, probably because of the poisoning action of impurities not removed from the commercial cholesterol. In such a case the addition of one or two 0.2-g. portions of catalyst usually suffices to bring the reaction practically to completion.

5. The sterol forms a hydrate from which the water is eliminated only after thorough drying, as in vacuum at 100°.

6. The acetyl derivative is more easily reduced than the free sterol.

7. Prepared by refluxing a solution of 5 g. of cholesterol in 7.5 cc. of acetic anhydride for one hour, cooling, and washing the crystalline product with cold methanol; yield 5 g., m.p. 114–115°.

8. Test for cholesterol: about 5 mg. of material is dissolved in 2 cc. of carbon tetrachloride; 1 cc. of acetic anhydride and 3–4 drops of concentrated sulfuric acid are added. Cholesterol gives a succession of color changes.

3. Methods of Preparation

Dihydrocholesterol has been prepared by the reduction of cholestenone with sodium and amyl alcohol[2] and by the hydrogenation of cholesterol. In the presence of platinum black or platinum oxide, yields varying from 6.5 per cent to 40 per cent have been obtained in ether,[3] acetone,[4] ethyl acetate,[5] and acetic acid.[6]

[1] Anderson and Nabenhauer, J. Am. Chem. Soc. **46**, 1957 (1924).

[2] Diels and Abderhalden, Ber. **39**, 889 (1906); Diels and Stamm, ibid. **45**, 2230 (1912); Neuberg, ibid. **39**, 1155 (1906).

[3] Willstätter and Mayer, ibid. **41**, 2200 (1908); Dorée, J. Chem. Soc. **95**, 644, (1909); Boehm, Biochem. Z. **33**, 474 (1911); Windaus and Uibrig, Ber. **47**, 2386 (1914); Ellis and Gardner, Biochem. J. **12**, 72 (1918); Anderson, J. Biol. Chem. **71**, 411 (1926); Vavon and Jakubowicz, Bull. soc. chim. [4] **53**, 584 (1933); Ruzicka, Brüngger, Eichenberger, and Meyer, Helv. Chim. Acta **17**, 1407 (1934).

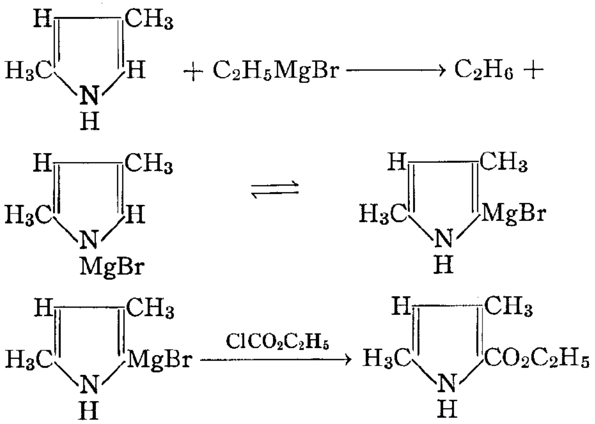
[4] Nord, Biochem. Z. **99**, 265 (1919).

[5] Shriner and Ko, J. Biol. Chem. **80**, 6 (1928).

[6] v. Fürth and Felsenreich, Biochem. Z. **69**, 420 (1915).

XVI

2,4-DIMETHYL-5-CARBETHOXYPYRROLE



Submitted by Hans Fischer.
Checked by C. R. Noller.

1. Procedure

In a 1-l. round-bottomed, three-necked flask fitted with an efficient reflux condenser, liquid-sealed stirrer, and dropping funnel is placed 13 g. (0.53 gram atom) of magnesium turnings. A few cubic centimeters of a solution of 60 g. (41.4 cc., 0.55 mole) of pure ethyl bromide in 50 cc. of absolute ether is added and the stirrer started (Note 1). When the bromide begins to react 200 cc. of absolute ether is added, and then the balance of the bromide solution is run in as fast as the refluxing permits (about one-half hour). After allowing fifteen minutes for the completion of the reaction, a solution of 40 g. (0.42 mole) of 2,4-dimethylpyrrole (Org. Syn. **15**, 20) in 100 cc. of absolute ether is added in the course of twenty minutes (Note 2) and the mixture is refluxed for one-half hour on the steam bath.

After cooling to room temperature, a solution of 58 g. (51 cc., 0.53 mole) of freshly distilled ethyl chloroformate (b.p. 92.5–93.5°) in 100 cc. of absolute ether is added dropwise in the course of one-half hour (Note 3). The mixture is heated on the steam bath for one and one-half hours and then allowed to stand overnight at room temperature.

The flask is placed in an ice-salt mixture and the contents decomposed by the gradual addition of 300 cc. of saturated ammonium chloride solution and 100 cc. of water (Note 4). The aqueous layer is removed by means of a 1500-cc. separatory funnel and sufficient ether is added to dissolve the yellow precipitate. The total volume of ether solution is about one liter. This is washed with two 200-cc. portions of water, and the three aqueous layers are extracted consecutively with a 100-cc. portion of ether. The combined ether solution is dried over 30 g. of anhydrous sodium sulfate, concentrated on the steam bath to a volume of about 200 cc., and cooled to room temperature. The product which crystallizes is collected with suction and washed with two 25-cc. portions of ether. The yield is 35–38 g. of light yellow product, m.p. 122–123°. The ether is completely removed from the combined filtrates by heating on the steam bath, and the black oil is allowed to stand overnight. The semi-solid mass is filtered with suction and washed with a minimum amount of cold ether. In this way an additional 6–7 g. of yellow material is obtained which melts at 119–121°.

The combined crude material is crystallized from 75 cc. of 95 per cent alcohol, and yields 37–39 g. of slightly colored material, m.p. 123–124°. A second crystallization from alcohol gives 34–36 g. of colorless product melting at the same temperature. By the systematic working of the alcoholic mother liquors, an additional 5–6 g. of pure material is obtained, making the total yield 40–41 g. (57–58 per cent of the theoretical amount).

2. Notes

1. Stirring is continued without interruption throughout the preparation to the point where the mixture is allowed to stand overnight.

2. The reaction is not exothermic, but the large volume of ethane evolved necessitates the regulated addition of the solution of dimethylpyrrole.

3. Considerable heat is produced during the addition of about two-thirds of the solution, after which the addition may be more rapid.

4. The first third of the ammonium chloride solution must be added quite slowly with frequent and thorough shaking.

3. Methods of Preparation

The most convenient laboratory method for the preparation of 2,4-dimethyl-5-carbethoxypyrrole is that given above.[1] A cheaper method of obtaining large quantities consists in the partial hydrolysis of 2,4-dimethyl-3,5-dicarbethoxypyrrole with sulfuric acid, followed by decarboxylation.[2] The ester has been obtained also by the alcoholysis of 5-trichloroaceto-2,4-dimethylpyrrole in the presence of sodium ethylate.[3] The free acid has been obtained from 1-[2,4-dimethylpyrrole-5]-2,4-dimethylpyrrole-5-carboxylic acid[4] and from 2,4-dimethylpyrrole-5-aldehyde.[5]

[1] H. Fischer, Weiss, and Schubert, Ber. **56**, 1199 (1923); Ingraffia, Gazz. chim. ital. **63**, 584 (1933).

[2] H. Fischer and Walach, Ber. **58**, 2820 (1925).

[3] Houben and W. Fischer, ibid. **64**, 2639 (1931).

[4] Magnanini, ibid. **22**, 38 (1889).

[5] Alessandri, Atti accad. Lincei **24** II 199 (1915); Alessandri and Passerini, Gazz. chim. ital. **51**, I 277 (1921).

XVII

β,β-DIPHENYLPROPIOPHENONE

$$C_6H_5CH{=}CHCOC_6H_5 + C_6H_6 \xrightarrow{(AlCl_3)} (C_6H_5)_2CHCH_2COC_6H_5$$

Submitted by P. R. Shildneck.
Checked by C. R. Noller and C. R. Kemp.

1. Procedure

In a 3-l. round-bottomed, three-necked flask fitted with a liquid-sealed mechanical stirrer, a thermometer, and a 500-cc. separatory funnel are placed 1700 cc. of dry benzene and 160 g. (1.2 moles) of powdered, anhydrous aluminum chloride (Note 1). The mixture is cooled to 10° by means of an ice-water bath and maintained at 10–20° during the addition of a solution of 120 g. (0.58 mole) of benzalacetophenone (Note 2) (Org. Syn. Coll. Vol. **1**, 71) in 300 cc. of dry benzene. This addition requires about thirty minutes. The cooling bath is then removed and stirring continued at room temperature until all the dense, yellow precipitate formed at first has gone into solution (Note 3). The reaction is complete after stirring for an additional hour.

The bulk of the brown-colored benzene solution is decanted into a cold mixture of 100 cc. of concentrated hydrochloric acid and 1500 cc. of water in a 5-l. round-bottomed flask. The remainder is filtered on a Büchner funnel, and the lumps of aluminum chloride are washed with two 100-cc. portions of benzene. The filtrates are added to the main solution and the whole is washed thoroughly with the dilute acid. If the layers do not separate readily the mixture is filtered with gentle suction and the water separated by siphoning. The solution is washed twice with 1500-cc. portions of water and filtered again if necessary.

The clear, light yellow benzene solution is subjected to rapid steam distillation (Note 4) in the same 5-l. flask, and when no more benzene passes over the flask is cooled under the tap with shaking. The residual oil solidifies to light brown pellets. These are collected, separated from water as much as possible, and dissolved in 2250 cc. of boiling alcohol. Five grams of decolorizing carbon is added; the hot solution is filtered with suction and allowed to cool. The best results are obtained if the alcoholic solution is stirred slowly with a mechanical stirrer while cooling to room temperature. Stirring is stopped when the mixture becomes semi-solid, and the mass is then allowed to stand for twenty-four hours. The fine, colorless needles are filtered on a 15-cm. Büchner funnel and pressed as dry as possible. The yield of thoroughly air-dried, colorless material melting at 91–92° (Note 5) amounts to 125–140 g. (76–85 per cent of the theoretical amount) (Note 6).

2. Notes

1. Trial runs demonstrated that one mole of benzalacetophenone required at least two moles of anhydrous aluminum chloride to complete the reaction at room temperature. When less aluminum chloride was used the yellow addition product failed to dissolve entirely even after stirring for twenty-four hours, and the yield was decreased.

2. The benzalacetophenone must be quite pure (m.p. 55–56°) and, in particular, free from benzaldehyde.

3. A change in appearance of the mixture is very noticeable at the end of the reaction. The yellow color rapidly gives way to a dark brown. A perfectly clear solution is not produced as the aluminum chloride remains in suspension.

4. If the benzene solution is steam-distilled directly from the acid mixture the crude product is darker in color, more difficult to crystallize, and less pure after crystallization.

5. The melting point of β,β-diphenylpropiophenone is given in the literature[1,2,3] as 96°. The product melting at 91–92° was recrystallized to constant melting point from alcohol and from ligroin but the melting point remained at 92° (corr.). The oxime and monobromide prepared according to Kohler[2] were found to melt at 133° (corr.) and 166° (corr.) respectively.

6. An additional 12–16 g. of less pure product, melting at 88–91°, may be obtained by concentrating the mother liquor to 400 cc.

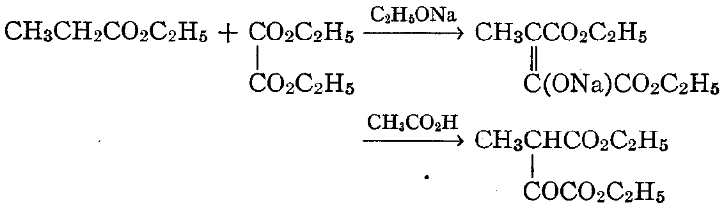
3. Methods of Preparation

β,β-Diphenylpropiophenone has been prepared from benzalacetophenone and phenylmagnesium bromide,[1] by the condensation of benzalacetophenone and benzene with concentrated sulfuric acid[2] or with aluminum chloride,[3] and by the action of aluminum chloride on a mixture of benzene and the hydrochloride of benzalacetophenone.[3] The procedure described here is essentially that of Vorländer and Friedberg.[3]

[1] Kohler, Am. Chem. J. **29**, 352 (1903).
[2] Kohler, ibid. **31**, 642 (1905).
[3] Vorländer and Friedberg, Ber. **56** 1144 (1923).

XVIII

ETHYL ETHOXALYLPROPIONATE



Submitted by RICHARD F. B. COX and S. M. MCELVAIN.
Checked by REYNOLD C. FUSON and WILLIAM E. ROSS.

1. Procedure

SIXTY-NINE grams (3 gram atoms) of sodium is powdered under xylene in a 3-l. three-necked flask. The mixture is cooled, the xylene is decanted, and the sodium is washed twice with small portions of dry ether. One liter of absolute ether is then added to the powdered sodium. The flask is fitted with a mercury-sealed stirrer, an efficient reflux condenser, and a dropping funnel, each of the latter being protected from moisture with a calcium chloride tube. One hundred and thirty-eight grams (175 cc., 3 moles) of absolute ethyl alcohol is added drop by drop through the funnel (Note 1). After the alcohol has been added and there is no unchanged sodium (as evidenced by cessation of boiling) the flask is immersed in an ice-water bath, and a mixture of 306 g. (342 cc., 3 moles) of ethyl propionate and 438 g. (404 cc., 3 moles) of ethyl oxalate is added slowly through the dropping funnel (Note 2).

After the ester mixture has been added, the stirrer is removed and the condenser set for downward distillation. The ether and the alcohol formed in the reaction are removed by heating on a water bath (Note 3). The residue, which usually solidifies

upon cooling, is treated with 600 cc. of cold, 33 per cent acetic acid solution. The mixture is allowed to stand for several hours with occasional shaking in order to decompose the sodium derivative completely, and the product is extracted with four 500-cc. portions of ether. The ether solution is washed with 1 l. of water, with two 500-cc. portions of 10 per cent sodium bicarbonate solution, and finally with 1 l. of water. The ether is then removed by distillation, using a steam bath. The residue is fractionated through an efficient column (Note 4). The portion boiling at 114–116°/10 mm. is collected. The yield is 363–425 g. (60–70 per cent of the theoretical amount).

2. Notes

1. The addition of the alcohol takes from four to six hours, depending on the efficiency of the condenser and stirrer.

2. The addition of the ester mixture should be slow enough so that the ether does not reflux. This addition takes two to three hours.

3. When most of the alcohol has distilled, a yellow scum forms on the surface of the red, viscous liquid. The distillation is stopped at this point. When the solution is cooled, the sodium derivative crystallizes with considerable expansion in volume.

4. No appreciable decomposition of the ethoxalyl ester into ethyl methylmalonate takes place when the distillation is carried out at 10 mm. To prevent overheating, the use of an oil bath and a heated column is recommended.

3. Methods of Preparation

Ethyl ethoxalylpropionate has been prepared by the Claisen condensation of ethyl oxalate with ethyl propionate [1] as above, and by the alkylation of ethyl ethoxalylacetate.[1]

[1] Wislicenus and Arnold, Ann. **246**, 329 (1888).

XIX

ETHYL METHYLMALONATE

$$\begin{array}{l} CH_3CHCO_2C_2H_5 \\ \quad | \\ \quad COCO_2C_2H_5 \end{array} \rightarrow CH_3CH(COOC_2H_5)_2 + CO$$

Submitted by RICHARD F. B. COX and S. M. MCELVAIN.
Checked by REYNOLD C. FUSON and WILLIAM E. ROSS.

1. Procedure

THREE HUNDRED AND FORTY-FIVE grams (1.7 moles) of ethyl ethoxalylpropionate, b.p., 114–116°/10 mm. (p. 54), is placed in a round-bottomed flask of suitable size carrying a reflux condenser, and a thermometer is suspended from the top of the condenser into the liquid. The ethyl ethoxalylpropionate is then heated until a vigorous evolution of carbon monoxide begins (130–150°). The temperature of the liquid is gradually raised as the gas evolution diminishes, and finally the liquid is refluxed until no more gas comes off. The ethyl methylmalonate is then distilled. It boils at 194–196°/745 mm., and the yield is 288 g. (97 per cent of the theoretical amount).

2. Methods of Preparation

The most widely used method of preparing ethyl methylmalonate is by the alkylation of ethyl malonate with methyl iodide,[1,2] methyl bromide,[3] or methyl sulfate.[4] A separation of the desired product from traces of unchanged starting material and from ethyl dimethylmalonate cannot be accomplished by distillation as the boiling points of the three esters lie within three and one-half degrees of one another. Michael [2] found that unchanged malonic ester can be removed completely by taking advantage of the greater ease with which it is hydrolyzed

by alkali, while Gane and Ingold [5] obtained a pure product by hydrolysis, crystallization of the methylmalonic acid, and re-esterification. It can be inferred from the results of Salkowski, jun.,[6] with acetoacetic ester that no disubstitution occurs when methyl bromide is employed as the alkylating agent. The pure ester can be prepared also from ethyl α-bromopropionate through the nitrile,[7] but the materials are expensive and the yields poor. The present method, which utilizes ethyl propionate and ethyl oxalate as the primary starting materials, was described first by Wislicenus.[8]

1 Zublin, Ber. **12**, 1112 (1879); Conrad and Bischoff, Ann. **204**, 146 (1880). Herzig and Wenzel, Monatsh. **24**, 115 (1903).

2 Michael, J. prakt. Chem. [2] **72**, 537 (1905).

3 Lucas and Young, J. Am. Chem. Soc. **51**, 2536 (1929).

4 Nef, Ann. **309**, 188 (1899).

5 Gane and Ingold, J. Chem. Soc. 14 (1926).

6 Salkowski, jun., J. prakt. Chem. [2] **106**, 256 (1923).

7 Zelinsky, Ber. **21**, 3162 (1888); Steele, J. Am. Chem. Soc. **53**, 283 (1931).

8 Wislicenus, Ber. **27**, 796 (1894).

XX

unsym.-HEPTACHLOROPROPANE

$$CCl_2{=}CCl_2 + CHCl_3 \xrightarrow{(AlCl_3)} CCl_3CCl_2CHCl_2$$

Submitted by Mark W. Farlow.
Checked by Frank C. Whitmore and F. W. Breuer.

1. Procedure

In a 1-l. round-bottomed flask equipped with a reflux condenser carrying a calcium chloride tube are placed 166 g. (103 cc., 1.0 mole) of technical tetrachloroethylene, 300 g. (200 cc., 2.5 moles) of dry chloroform, and 27 g. (0.2 mole) of anhydrous aluminum chloride. The mixture is refluxed gently on the steam bath for fifteen hours (Note 1), cooled to room temperature, and poured into a 1-l. separatory funnel half filled with crushed ice. The organic layer is washed several times with water and dried over calcium chloride or soluble anhydrite. By fractionation at atmospheric pressure through an efficient column 160–165 g. of chloroform is recovered. Distillation of the *unsym.*-heptachloropropane fraction at diminished pressure gives material boiling at 110–113°/10 mm., or 137–140°/32 mm., and melting at 29–30°. The yield is 250–266 g. (88–93 per cent of the theoretical amount) (Note 2).

2. Notes

1. A small amount of hydrogen chloride is evolved in the initial stages of the reaction.

2. According to Prins[1] the heptachloropropane can be isolated easily by pouring the reaction mixture into water and removing the unreacted materials by steam distillation. The process is stopped when the product begins to distil, and on cooling the residue is obtained as a colorless solid of the correct melting point.

3. Methods of Preparation

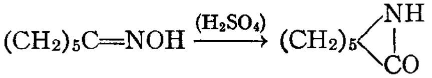
The method is essentially that discovered by Böeseken and Prins[2] and studied further by Prins.[1,3] Pentachloroethane can be used in place of tetrachlorethylene, as it is converted into the unsaturated compound in the presence of aluminum chloride. *unsym.*-Heptachloropropane has been obtained also by the action of phosphorus pentachloride on pentachloroacetone,[4] and by treating dichloroacetyl chloride with aluminum chloride.[5]

[1] Prins, Rec. trav. chim. **54**, 249 (1935).
[2] Böeseken and Prins, Chem. Zentr. I, 466 (1911).
[3] Prins, J. prakt. Chem. (2) **89**, 414 (1914).
[4] Fritsch, Ann. **297**, 312 (1897).
[5] Böeseken, Rec. trav. chim. **29**, 109 (1910).

XXI

2-KETOHEXAMETHYLENIMINE

(ϵ-Caprolactam)



Submitted by C. S. Marvel and J. C. Eck.
Checked by L. F. Fieser and C. H. Fisher

1. Procedure

The rearrangement of 120 g. (1.06 moles) of pure cyclohexanoneoxime (Org. Syn. 11, 56) (Note 1) is carried out in the following fashion. In a 250-cc. Erlenmeyer flask are placed 10 g. of cyclohexanoneoxime and 20 cc. of sulfuric acid (sp. gr. 1.783) (Note 2). The flask is placed on a wire gauze over a small free flame and heated slowly, with occasional shaking, until the first appearance of bubbles. The flame is then removed immediately, and the very vigorous exothermic reaction which occurs is allowed to run to completion (Note 3). This requires only a few seconds. This solution is then poured into a 3-l. round-bottomed flask, and another 10-g. portion of the oxime is introduced into the Erlenmeyer flask and treated with sulfuric acid as before. These operations are repeated until the twelve 10-g. portions have been treated.

The 3-l. flask containing the dark-colored sulfuric acid solution of the lactam is fitted with a mechanical stirrer and a separatory funnel and packed in an ice-salt mixture. The solution is cooled to 0° and carefully made faintly alkaline to litmus by the addition of 24 per cent potassium hydroxide solution, added very slowly (five to six hours) with good cooling (Note 4). Usually about 1550 cc. of the alkaline solution is needed. The tempera-

ture must be kept below 10° to avoid hydrolysis during this stage of the preparation.

The potassium sulfate which has separated is then removed by filtration and washed with two 100-cc. portions of chloroform. The faintly alkaline aqueous solution is extracted with about five 200-cc. portions (Note 5) of chloroform, and the combined chloroform solutions are washed once with 50 cc. of water to remove any alkali. The chloroform is then distilled and the product fractionated under reduced pressure. The yield of 2-ketohexamethylenimine, boiling at 127–133°/7 mm. and melting at 65–68°, amounts to 71–78 g. (59–65 per cent) (Note 6).

2. Notes

1. Pure cyclohexanoneoxime, m.p. 86–88°, must be used since poorer grades char badly when treated with sulfuric acid.

2. This concentration of sulfuric acid is obtained by mixing concentrated sulfuric acid (sp. gr. 1.84) with water in the ratio of 5 cc. to 1 cc.

3. After the first appearance of bubbles, the flask should not be shaken until the reaction has spread through the entire solution as the reaction may subside and then later become violent. Larger quantities of oxime should not be used in a single run since excessive charring takes place.

4. Potassium hydroxide gives better results than does sodium hydroxide since, if the latter is used, the large amount of hydrated sodium sulfate which separates from the solution prevents efficient cooling.

5. The extraction is continued until no appreciable amount of product is obtained in the chloroform layer.

6. The literature reports the boiling point as 139–140°/12 mm. and the melting point at various temperatures from 65° to 70°.

3. Methods of Preparation

2-Ketohexamethylenimine has been obtained by heating ϵ-aminocaproic acid or its ethyl ester [1] and by the rearrangement of cyclohexanoneoxime.[2,3,4] The method [4] described above is

Ruzicka's [3] modification of Wallach's [2] original directions for the rearrangement of the oxime.

[1] Gabriel and Maass, Ber. **32**, 1271 (1899); von Braun, Ber. **40**, 1840 (1907); Carothers and Berchet, J. Am. Chem. Soc. **52**, 5289 (1930).
[2] Wallach, Ann. **312**, 187 (1900); **343**, 43 (1905).
[3] Ruzicka, Seidel, and Hugoson, Helv. Chim. Acta **4**, 477 (1921).
[4] Eck and Marvel, J. Biol. Chem. **106**, 387 (1934).

XXII

6-METHYLURACIL

$$NH_2CONH_2 + CH_3COCH_2COOC_2H_5 \rightarrow CH_3C(NHCONH_2){=}CHCOOC_2H_5 + H_2O$$

$$CH_3C(NHCONH_2){=}CHCOOC_2H_5 + NaOH \rightarrow CH_3C(NHCONH_2){=}CHCOONa + C_2H_5OH$$

$$CH_3C(NHCONH_2){=}CHCOONa + HCl \rightarrow CH_3\overset{|}{C}{=}CH{-}\overset{|}{C}O\ (\text{NH-CO-NH}) + H_2O + NaCl$$

Submitted by John J. Donleavy and Mearl A. Kise.
Checked by Reynold C. Fuson and William E. Ross.

1. Procedure

Eighty grams (1.33 moles) of finely powdered urea is stirred into a mixture of 160 g. (155 cc., 1.23 moles) of ethyl acetoacetate (Note 1), 25 cc. of absolute alcohol (Note 2), and ten drops of concentrated hydrochloric acid in a 5-in. crystallizing dish. The reagents are mixed well and the dish is covered loosely with a watch glass and placed in a vacuum desiccator over concentrated sulfuric acid. The desiccator is evacuated continuously with a water pump until the mixture has gone to dryness (Note 3), which usually requires from five to seven days (Note 4). The crude β-uraminocrotonic ester when thoroughly dry weighs 200–205 g.

The dry, finely powdered, crude β-uraminocrotonic ester is stirred into a solution of 80 g. (2 moles) of sodium hydroxide in 1200 cc. of water at 95°. The clear solution is then cooled to 65° and carefully acidified, while stirring, by the slow addition of concentrated hydrochloric acid. The 6-methyluracil precipitates almost immediately, and after the mixture is cooled the product is collected on a filter, washed with cold water, alcohol, and ether, and air-dried. The substance is obtained as a colorless

powder of a high degree of purity, and the yield is 110–120 g. (71–77 per cent of the theoretical amount). For further purification the pyrimidine may be crystallized from glacial acetic acid. 6-Methyluracil decomposes above 300°.

2. Notes

1. Commercial ethyl acetoacetate can be used with satisfactory results.

2. Larger amounts of alcohol increase the period of drying without improving the yield. When no alcohol is used, the condensation proceeds slowly and the yields are low.

3. If the condensation product is used before it is dry, a large amount of carbon dioxide is evolved later in the course of the acidification, indicating incomplete utilization of the ethyl acetoacetate.

4. It is usually advisable to change the sulfuric acid at least daily. Any lumps should be disintegrated occasionally to aid in the drying process.

3. Methods of Preparation

The synthesis of 6-methyluracil from ethyl acetoacetate and urea was described first by Behrend.[1] The substance has been obtained also by the action of lead hydroxide on methylthiouracil in an alkaline medium,[2] and by boiling benzalmethylhydroxypyrimidinhydrazine with hydrochloric acid.[3]

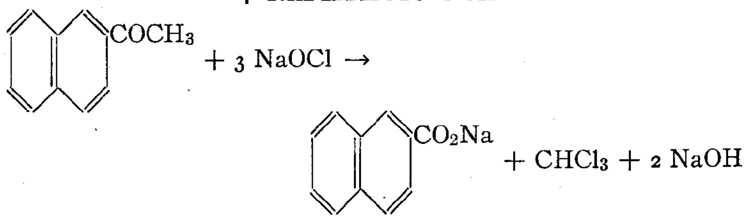
[1] Behrend, Ann. **229**, 5 (1885); Behrend and Roosen, ibid. **251**, 238 (1889). See also Biltz and Heyn, ibid. **418**, 109 (1916).

[2] List, ibid. **236**, 23 (1886).

[3] Thiele and Bihan, ibid. **302**, 308 (1898).

XXIII

β-NAPHTHOIC ACID



$$C_{10}H_7CO_2Na + HCl \rightarrow C_{10}H_7CO_2H + NaCl$$

Submitted by M. S. Newman and H. L. Holmes.
Checked by W. W. Hartman and F. W. Jones.

1. Procedure

In a 3-l. flask are placed a solution of 184 g. (4.6 moles) of sodium hydroxide in 300–400 cc. of water and sufficient ice to make the total volume about 1500 cc. Chlorine is passed into the solution, keeping the temperature below 0° by means of a salt-ice bath, until the solution is neutral to litmus (Note 1). After the addition of a solution of 34 g. of sodium hydroxide in 50 cc. of water, the flask is supported by a clamp and equipped with a thermometer and an efficient stirrer. The solution is warmed to 55°, and 85 g. (0.5 mole) of methyl β-naphthyl ketone (Note 2) is added. The mixture is vigorously stirred and, after the exothermic reaction commences, the temperature is kept at 60–70° (Note 3) by frequent cooling in an ice bath until the temperature no longer tends to rise. This requires thirty to forty minutes. The solution is stirred for thirty minutes longer and then the excess hypochlorite is destroyed by adding a solution of 50 g. of sodium bisulfite in 200 cc. of water (Note 4). After cooling to room temperature, the reaction mixture is transferred to a 4-l. beaker and carefully acidified with 200 cc.

of concentrated hydrochloric acid. The crude colorless acid is collected on a Büchner funnel, washed with water, and sucked as dry as possible with a rubber dam. After drying, the acid is crystallized (Note 5) from 600 cc. of 95 per cent alcohol, giving 75–76 g. (87–88 per cent of the theoretical amount) of β-naphthoic acid melting at 184–185° (corr.). By distilling 450 cc. of solvent from the mother liquor, an additional 9 g. (10 per cent of the theoretical amount) of acid, m.p. 181–183° (corr.), is obtained (Note 6).

2. Notes

1. The hypochlorite solution also may be prepared conveniently from the calcium hypochlorite sold by the Mathieson Alkali Works under the trade name "HTH" and specified to contain not less than 65 per cent of available calcium hypochlorite.

In a 3-l. round-bottomed flask 250 g. of commercial calcium hypochlorite is dissolved in 1 l. of warm water and a warm solution of 175 g. of potassium carbonate and 50 g. of potassium hydroxide in 500 cc. of water is added. The flask is stoppered and shaken vigorously until the semi-solid gel which first forms become quite fluid. The suspended solid is removed by filtration on a large Büchner funnel, washed with 200 cc. of water, and sucked as dry as possible with the aid of a rubber dam and an efficient suction pump. The filtrate of approximately 1500 cc. is placed in a 3-l. round-bottomed flask and is ready for the addition of methyl β-naphthyl ketone.

Such a solution contains approximately 200 g. (2.3 moles) of potassium hypochlorite. Sodium or potassium hypochlorite may be used, but the calcium salt is not satisfactory because the calcium salt of β-naphthoic acid is sparingly soluble.

2. The Eastman product, m.p. 53–55°, was used.

3. If the mixture is not cooled, the reaction will get out of control because of the rapid evolution of chloroform, and some ketone may steam-distil.

4. It is advisable to test the solution after the addition of the sodium bisulfite with acidified potassium iodide solution to be sure that all the hypochlorite has been destroyed. If hypochlorite is present, the chlorine liberated when the solution is acidified forms a high-melting impurity.

5. The moist acid may be crystallized without drying, but in doing so more alcohol must be used to get the product into solution.

6. This method may be used for the preparation of larger quantities, a batch twenty times this size giving a yield of 87 per cent. It may be used also for the preparation of other aromatic acids where suitable ketones are available. Methyl α-naphthyl ketone prepared by Caille's method [1] is not suitable for the preparation of α-naphthoic acid as it contains at least 30 per cent of the methyl β-naphthyl ketone.[2,3]

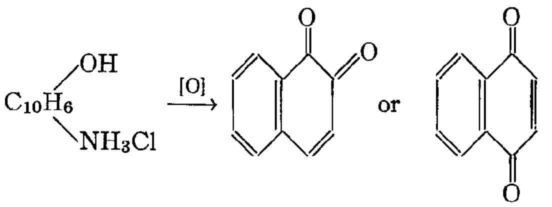
3. Methods of Preparation

β-Naphthoic acid has been prepared principally by the hydrolysis of β-naphthonitrile;[4] the overall yields from β-naphthylamine, from sodium-β-naphthalene sulfonate, and from calcium β-naphthalene sulfonate being given as (approximately) 20 per cent, 21 per cent, and 50 per cent, respectively.[5] The acid has been prepared also by the carbonation of the Grignard reagent from the less accessible β-bromo derivative [6] and, more recently, from the readily available methyl ketone.[3]

[1] Caille, Compt. rend. **153**, 393 (1911).
[2] St. Pfau and Ofner, Helv. Chim. Acta **9**, 669 (1926).
[3] Fieser, Newman, and Holmes, J. Am. Chem. Soc. **58**, 1055 (1936).
[4] Baeyer and Besemfelder, Ann. **266**, 187 (1891).
[5] Derick and Kamm, J. Am. Chem. Soc. **38**, 408 (1916).
[6] Gilman and St. John, Rec. trav. chim. **48**, 743 (1929).

XXIV

β-NAPHTHOQUINONE AND α-NAPHTHOQUINONE



Submitted by Louis F. Fieser.
Checked by C. R. Noller and W. R. White.

1. Procedure

(*A*) *β-Naphthoquinone.*—For the best results this preparation must be carried out rapidly. The vessels and reagents required should be made ready in advance. The oxidizing solution is prepared by dissolving 240 g. (0.89 mole) of ferric chloride hexahydrate in a mixture of 90 cc. of concentrated hydrochloric acid and 200 cc. of water with heating, cooling to room temperature by the addition of 200–300 g. of ice, and filtering the solution by suction.

Eighty grams (0.41 mole) of 1,2-aminonaphthol hydrochloride of a high degree of purity (Note 1) is placed in a 5-l. round-bottomed flask and covered with a solution of 5 cc. of hydrochloric acid in 3 l. of water which has been heated to 35°. The material is dissolved quickly by shaking (one to two minutes), and the solution is filtered rapidly by suction from a trace of residue and transferred to a clean 5-l. flask (Note 2). The oxidizing solution is added all at once while rotating the flask vigorously in order to mix the two solutions thoroughly. The quinone separates at once as a voluminous, microcrystalline, yellow precipitate. The product is collected on a Büchner funnel, washed well with water (Note 3), and then for more thorough

washing it is transferred to a large beaker, stirred for a few minutes with 2 l. of water (at 30°), and again collected. The filter cake is cut into slices and dried on filter paper at room temperature in an atmosphere free from acid fumes. The yield is 60–61 g. (93–94 per cent of the theoretical amount).

The material is pure golden yellow in color and melts with decomposition at 145–147°, with some softening at about 140°. It contains none of the black, sparingly soluble dinaphthyl-diquinhydrone and dissolves without residue in alcohol or benzene. Under the microscope it is seen to consist of a mass of well-formed, fine needles. By crystallization from alcohol or benzene it may be obtained as orange-red needles of good appearance, but the process is unreliable, it involves much loss of material, and the point of decomposition is lowered by 10–20°. It is thus best to use or to preserve the quinone in the form originally obtained; in this condition it is essentially pure and it will keep indefinitely. The material should not be pulverized, for it then becomes highly electrified.

(*B*) *α-Naphthoquinone.*—A mixture of 70 g. (0.36 mole) of pure 1,4-aminonaphthol hydrochloride (Note 4) and 2100 cc. of water at 30° in a 5-l. flask is stirred for a few minutes in order to dissolve most of the material and then treated with 100 cc. of concentrated sulfuric acid. The mixture is heated to the boiling point until all the precipitated amine sulfate has been brought into solution. The solution is somewhat pink. The hot solution is poured rapidly through a large funnel (without a paper), which has been warmed on the steam bath, into a 5-l. round-bottomed flask containing a filtered solution at room temperature of 70 g. (2.4 moles) of potassium dichromate in 1 l. of water. The flask is shaken to mix the contents thoroughly. The quinone separates at once as a mass of fine, yellow needles. After cooling to 25° the material is collected, washed with water, and dried at 30–40°. The crude product is dull yellow; it melts at 124–125° to a dark liquid and weighs 53–55 g. (Note 5).

The crude naphthoquinone is warmed gently on the steam bath with 1.5 l. of ether, when it rapidly dissolves and leaves in suspension a slight amount of dark, fluffy material. The solution

is shaken for ten minutes with 10 g. of decolorizing carbon; it is then filtered and the ether is distilled from a steam bath until crystals begin to form. The solution is then allowed to cool undisturbed, and the clear, canary-yellow prisms which separate are collected and washed with ether. The mother liquor is clarified by shaking as before with 7 g. of decolorizing carbon, filtered, and evaporated to a small volume until crystals begin to separate. The crystals are again washed with ether, and the mother liquor is clarified and evaporated once more. The final crop of material is dull in color but yields a pure product on recrystallization. All the material is of a high quality and melts at 124–125° to a clear yellow liquid; the yield is 44–46 g. (78–81 per cent of the theoretical amount).

2. Notes

1. The quality of the β-naphthoquinone is highly dependent upon the purity of the starting material. The crystalline product described on p. 10 may be used without recrystallization and, indeed, without being dried. The excess of oxidizing agent specified is sufficient to allow for a yield of aminonaphthol slightly higher than that given; if the yield is lower the larger excess of ferric chloride does no harm.

2. The solution at this point should be clear, but it may acquire a rather pronounced orange-yellow color when viewed in bulk. It should not, however, turn purple.

3. The yellow color of the wash water is due to a slight solubility of the quinone.

4. The recrystallized material described on p. 12 was used. It is not necessary to dry and weigh the hydrochloride before carrying out the oxidation.

5. The method of oxidation is essentially that of Russig.[1] The product obtained is slightly but definitely better than that produced at a lower temperature, or by adding the sulfuric acid to the dichromate solution, or by using ferric chloride as in (*A*). These latter procedures give the same yield, but the product is less pure and contains a black, ether-soluble impurity which must be washed out carefully after crystallization from ether.

3. Methods of Preparation

The only satisfactory method of preparing β-naphthoquinone is by the oxidation of 1,2-aminonaphthol in acid solution, and the chief problem involved is that of the preparation of this intermediate in suitable yield and purity. This problem and the literature pertaining to it are discussed elsewhere.[2] Most reports of the preparation of the aminonaphthol include some description of its oxidation, but the only particularly helpful comment on the reaction is that ferric chloride is a better oxidizing agent than chromic acid because at a low temperature it does not attack the quinone, even when present in excess.[3]

One other method is from 1,2-bromonaphthol through the keto-nitrobromide.[4] Though the parent quinone itself is such a sensitive compound that the material so obtained decomposed within a few hours, the method is of considerable value for the preparation of certain substituted β-naphthoquinones.[5]

α-Naphthoquinone is best prepared from 1,4-aminonaphthol, and the references [2] to the preparation of this intermediate also apply in most cases to the oxidation. A second method, and one which, although somewhat tedious, was used with success by a number of early investigators, is by the oxidation of naphthalene with chromic anhydride.[6] The procedure has been worked out in detail,[7] and the yield amounts to as much as 16 per cent of the theoretical quantity. For the preparation of certain homologues[8] and substitution products[9] this is by far the best method available. No advantage is gained by using α-naphthol or α-naphthylamine [10] in place of naphthalene. Frequent reference has been made in the patent literature to the formation of α-naphthoquinone, along with phthalic anhydride, on the catalytic or electrochemical oxidation of naphthalene, but it has not been demonstrated that this is a satisfactory method of preparation.

Most investigators have purified α-naphthoquinone by steam distillation, but for the efficient handling of any but very small quantities it appears necessary to use superheated steam in vacuum,[11] and the recovery amounts to only 70 per cent.

Crystallization from ligroin has been found to be very tedious,[12] and purification with benzene-ligroin has been declared both difficult and unsatisfactory.[11]

When just a trace of dark impurity is present, as in some of the commercial preparations, a completely pure product is easily obtained by vacuum distillation,[13] but the ordinary crude reaction product is likely to decompose when treated in this manner. The ether method introduced in the present procedure [14] has the advantage of being simple and efficient. It is equally applicable to the purification of the homologues of α-naphthoquinone.

[1] Russig, J. prakt. Chem. (2) **62**, 31 (1900).
[2] Org. Syn. **17**, 14.
[3] Groves, J. Chem. Soc. **45**, 298 (1884).
[4] Fries, Ann. **389**, 315 (1912).
[5] Fries and Schimmelschmidt, ibid. **484**, 245 (1930).
[6] Groves, J. Chem. Soc. **26**, 209 (1873).
[7] Plimpton, ibid. **37**, 634 (1880); Japp, ibid. **39**, 220 (1881); Miller, Ber. **17R**, 355 (1884).
[8] Weissgerber and Kruber, ibid. **52**, 346 (1919).
[9] Kegel. Ann. **247**, 178 (1888); Fieser and co-workers, J. Am. Chem. Soc. **56**, 2690 (1934); **58**, 572 (1936).
[10] Monnet, Reverdin, and Nölting, Ber. **12**, 2306 (1879).
[11] Conant and Freeman, Org. Syn. Coll. Vol. **1**, 375 (1932).
[12] Zincke and Wiegand, Ann. **286**, 70 (1895).
[13] Fieser and Peters, J. Am. Chem. Soc. **53**, 4089 (1931).
[14] Fieser and Fieser, ibid. **57**, 491 (1935).

XXV

PENTAERYTHRITYL BROMIDE AND IODIDE

(*sym.*-Tetrabromo- and Tetraiodo-*neo*-pentane)

$$3\ C(CH_2OH)_4 + 4\ PBr_3 \rightarrow 3\ C(CH_2Br)_4 + 4\ H_3PO_3$$

$$C(CH_2Br)_4 + 4\ NaI \rightarrow C(CH_2I)_4 + 4\ NaBr$$

Submitted by H. B. Schurink.
Checked by Wallace H. Carothers and W. L. McEwen.

1. Procedure

(*A*) *Pentaerythrityl Bromide.*—One hundred and twenty-five grams (0.92 mole) of dry pentaerythritol (Org. Syn. Coll. Vol. 1, 417) is placed in a 500-cc. round-bottomed flask provided with an air-cooled reflux condenser bearing at the upper end a long-stemmed dropping funnel and a bent glass tube. The tube is connected to a suitable trap (Org. Syn. Coll. Vol. 1, 91; Org. Syn. 14, 2) for absorbing the large quantity of hydrogen bromide which is evolved. The flask is heated on a steam bath, and 500 g. (173 cc., 1.85 moles) of freshly distilled phosphorus tribromide (Org. Syn. 13, 21) is added cautiously from the dropping funnel. When this addition has been completed the steam bath is replaced by an oil bath and the temperature is raised gradually to 170–180° (Note 1). After heating at this point for twenty hours, the orange-red reaction mixture is transferred to a beaker containing 1 l. of cold water and stirred thoroughly to reduce the lumps to a small size. The red, flocculent material is filtered with suction and washed several times with hot water; finally it is washed thoroughly with two 200-cc. portions of cold 95 per cent ethyl alcohol (Note 2). After drying, the material is transferred to a large Soxhlet extractor and extracted exhaustively with 95 per cent alcohol (Note 3). The pentaerythrityl

bromide separates from the alcohol and after cooling is collected with suction. The yield of crude product melting at 158–160° is 245–270 g. (69–76 per cent of the theoretical amount); this material is sufficiently pure for conversion to the iodide (Note 4). For purification, the crude product may be recrystallized from 95 per cent alcohol, using 30 cc. of solvent per gram; the melting point is raised to 163°, and the recovery is about 85 per cent.

(*B*) *Pentaerythrityl Iodide.*—In a 500-cc. round-bottomed flask fitted with a reflux condenser, a mixture of 100 g. (0.67 mole) of sodium iodide (dried at 120°), 300 cc. (240 g.) of ethyl methyl ketone (Note 5), and 50 g. (0.13 mole) of crude pentaerythrityl bromide (m.p. 158–160°) is refluxed on a steam bath for forty-eight hours. The condenser is set for distillation, the solvent is distilled, and the residue is washed into a hot Büchner funnel with hot water. The product is washed thoroughly on the funnel with boiling water, pressed well, and transferred to a large Soxhlet extractor. To remove impurities the material is submitted to extraction with boiling 95 per cent alcohol until a sample removed from the extraction thimble melts at 233° (Note 6). The product is then removed from the thimble and dried; the yield is 66–73 g. (89–99 per cent of the theoretical amount). The crude product may be recrystallized from hot benzene, using about 18 cc. of solvent per gram. The recovery is about 80 per cent, and the melting point is not changed.

2. Notes

1. The temperature must be raised slowly to avoid formation of spontaneously inflammable hydrides of phosphorus which will ignite and destroy the preparation. A similar result occurs if the phosphorus tribromide is added at 170°.

2. This washing eliminates intermediate bromohydrins.

3. Since the extraction is slow, it is advisable to divide the material into several portions and carry out a number of simultaneous extractions. The extractor used was a modified Soxhlet arranged so that the extractor tube is heated by the vapor of the solvent (Org. Syn. **16**, 69, Note 3).

4. The crude product has a disagreeable odor probably due to the presence of a compound of phosphorus. The odor may be eliminated by heating at 120°, followed by several recrystallizations.

5. Acetone may be used as solvent in place of ethyl methyl ketone, but the reaction must then be carried out in a sealed vessel at 95–100° for thirty to thirty-six hours.

6. The extraction requires twelve to sixteen hours, depending upon the rate of refluxing of the alcohol.

3. Methods of Preparation

Pentaerythrityl bromide has been prepared by the action of phosphorus tribromide on pentaerythritol,[1,2] and of an acetic acid solution of hydrobromic acid on pentaerythritol tetraacetate.[3] The iodide has been prepared by the action of red phosphorus and hydriodic acid on pentaerythritol[4] and by treating the bromide with sodium iodide in acetone.[2]

[1] Rave and Tollens, Ann. **276**, 61 (1893); Gustavson, J. prakt. Chem. [2] **54**, 98 (1896).

[2] Backer and Schurink, Rec. trav. chim. **50**, 921 (1931).

[3] Perkin and Simonsen, J. Chem. Soc. **87**, 860 (1905).

[4] Tollens and Wigand, Ann. **265**, 331 (1891).

XXVI

α-PHENYLETHYLAMINE

$$C_6H_5COCH_3 + 2\ HCO_2NH_4 \rightarrow C_6H_5CH(NHCHO)CH_3 + 2\ H_2O + NH_3 + CO_2$$

$$C_6H_5CH(NHCHO)CH_3 + H_2O + HCl \rightarrow C_6H_5CH(NH_3Cl)CH_3 + HCO_2H$$

$$C_6H_5CH(NH_3Cl)CH_3 + NaOH \rightarrow C_6H_5CH(NH_2)CH_3 + NaCl$$

Submitted by A. W. Ingersoll.
Checked by Reynold C. Fuson and William E. Ross.

1. Procedure

In a 500-cc. modified Claisen flask are placed 250 g. (4 moles) of ammonium formate (Note 1), 150 g. (145 cc., 1.25 moles) of acetophenone (Note 2) and a few chips of porous plate. The flask is fitted with a cork carrying a thermometer extending nearly to the bottom, and the side arm is connected to a small condenser set for distillation. On heating the flask with a small flame the mixture first melts to two layers and distillation occurs; at 150–155° it becomes homogeneous and reaction takes place with moderate foaming. The heating is continued, more slowly if necessary, until the temperature reaches 185°. During this process water, acetophenone, and ammonium carbonate distil; about three hours is required and little attention is necessary. At 185° the heating is stopped and the upper layer of acetophenone is separated from the distillate and returned, without drying, to the reaction flask. The mixture is then heated for three hours at 180–185°. The distillate is extracted with 25–30 cc. of benzene to recover acetophenone (Note 3), and the aqueous portion is discarded.

The reaction mixture is cooled and then shaken in a 500-cc. separatory funnel with 150–200 cc. of water to remove ammo-

nium formate and formamide. The crude α-phenylethylformamide is drawn off into the original flask and the water layer is extracted with two 30-cc. portions of benzene and discarded. The benzene extracts are united with the main portion, and 150 cc. of concentrated hydrochloric acid is added, together with a few pieces of porous plate. The mixture is cautiously heated until the benzene has distilled and then boiled gently for forty to fifty minutes longer. Hydrolysis proceeds rapidly and the mixture becomes homogeneous except for a small layer of acetophenone and other neutral substances. The mixture is cooled and extracted first with 50 cc. of benzene and then with three or four 25-cc. portions of the solvent. The extracts are saved for the recovery of acetophenone (Note 3).

The aqueous acid solution is transferred to a 1-l. round-bottomed flask provided with a separatory funnel and equipped for steam distillation. A solution of 125 g. of sodium hydroxide in 250 cc. of water is added through the funnel, and the mixture is distilled with steam (Note 4). The first liter of distillate contains most of the amine, but the distillate should be collected until it is only faintly alkaline. A small residue containing di-(α-phenylethyl)-amine and neutral substances remains in the flask and may be discarded.

The distillate is extracted with five 50-cc. portions of benzene, and the benzene solution is dried thoroughly with powdered sodium hydroxide and distilled (Note 5). Most of the amine distils at 184–186°, but the fraction distilling at 180–190° is sufficiently pure for most purposes (Note 6). The yield of this fraction is 80–88 g. By combining the benzene fore-run with the distillation residue, extracting with dilute acid, and recovering the amine as above, an additional 10–12 g. of material can be obtained (Note 7), making the total yield 90–100 g. (60–66 per cent of the theoretical amount based on the acetophenone taken) (Note 8).

2. Notes

1. Ammonium formate may be made in quantity by treating solid ammonium carbonate with a slight excess of commercial

85 per cent formic acid and concentrating the solution, in stages, on a steam bath under reduced pressure. The slightly moist product obtained by suction filtration is suitable for this preparation.

2. Eastman's "Practical" acetophenone, m.p. 16–20°, was used.

3. The benzene solution is washed with dilute alkali, dried, and distilled, the fraction boiling at 198–207° being collected.

4. In the steam distillation it is advisable to heat the distillation flask directly so that the volume remains nearly constant.

5. The amine attacks cork and rubber and absorbs carbon dioxide from the air. It is best distilled in a flask having an in-set side arm and collected in a distilling flask protected by a soda-lime tube.

6. If very pure amine is desired the product described above is dissolved with 1.04 parts of crystalline oxalic acid in eight parts of hot water. After clarification with Norite, the filtered solution on cooling deposits crystals of the acid oxalate. About 5 g. of the salt remains in each 100 cc. of the mother liquor; most of this can be obtained by evaporation and further crystallization. The amine is liberated from the pure oxalate with potassium hydroxide, distilled with steam, and purified as described above. When a known amount of amine is desired in water solution (as for optical resolution) a weighed amount of the (anhydrous) oxalate is decomposed and the amine is distilled quantitatively with steam.

7. When several runs are to be made the acid solution of the amine may be combined with the next run previous to steam distillation.

8. The method described is rather general. With appropriate modifications for the purification of the amine the method yields α-*p*-tolylethylamine (72 per cent), α-*p*-chlorophenylethylamine (65 per cent), α-*p*-bromophenylethylamine (63 per cent), α-*p*-xenylethylamine (66 per cent), and α-(β-naphthyl)-ethylamine (84 per cent) from the corresponding ketones.

3. Methods of Preparation

The present procedure was developed from those of Wallach [1] and Freylon,[2] based upon the general method discovered by Leuckart.[3] α-Phenylethylamine also can be prepared satisfactorily by the reduction of acetophenone oxime with sodium and absolute alcohol [4] or sodium amalgam,[5] but the reagents are more expensive and the processes less convenient. The amine has been obtained by reducing acetophenone oxime electrolytically,[6] by reducing acetophenone phenylhydrazone with sodium amalgam and acetic acid,[7] from α-phenylethyl bromide and hexamethylenetetramine,[8] and by the action of methylmagnesium iodide upon hydrobenzamide,[9] as well as by other methods of no preparative value.

[1] Wallach, Ann. **343**, 60 (1905).
[2] Freylon, Ann. chim. phys. (8) **15**, 141 (1908).
[3] Leuckart, Ber. **22**, 1413 (1889).
[4] Mohr, J. prakt. Chem. (2) **71**, 317 (1905).
[5] Kraft, Ber. **23**, 2783 (1890).
[6] Tafel and Pfeffermann, ibid. **35**, 1515 (1902).
[7] Tafel, ibid. **19**, 1929 (1886); **22**, 1856 (1889).
[8] André and Vernier, Compt. rend. **193**, 1192 (1931).
[9] Busch and Leefhelm, J. prakt. Chem. (2) **77**, 5 (1908).

XXVII

d- AND *l*-α-PHENYLETHYLAMINE

Submitted by A. W. INGERSOLL.
Checked by REYNOLD C. FUSON and WILLIAM E. ROSS.

1. Procedure

d-α-Phenylethylamine.—A solution of 100 g. (0.75 mole) (Note 1) of *l*-malic acid in 500 cc. of distilled water is mixed with 120 g. (1 mole) of *dl*-α-phenylethylamine (p. 76); the resulting solution is heated for a short time on the steam bath, filtered into a 1-l. beaker, and allowed to cool slowly. After several hours the crude *d*-α-phenylethylamine-*l*-malate which crystallizes is collected by suction filtration and washed on the filter with 25 cc. of ice water. The filtrate and washings are evaporated on a steam bath to a volume about two-thirds that of the filtrate, and a second crop of crystals is obtained on cooling (Notes 2 and 3). By repeating the process it is possible to obtain a third and usually a fourth crop, after which the mother liquor becomes too viscous to permit satisfactory crystallization. The mother liquor is reserved for later use.

The successive crops of crystals are systematically recrystallized as follows, using Norite if necessary. About two-thirds of the first crop is dissolved in about three parts of water and the hot solution allowed to deposit crystals by slow cooling (Note 3). The liquor is filtered or decanted, the remainder of the first crop is dissolved in it, and the process of crystallization is repeated. The remaining crops are then similarly recrystallized in succession from the same liquor, the solution being evaporated to the appropriate volume before each crystallization. The final mother liquor is evaporated in stages and the viscous residue is united with that from the original crystallization. The various crops are systematically recrystallized from fresh water until pure

(Note 4). It is possible to obtain 80–90 g. (63–70 per cent of the theoretical amount) of the pure *d*-base-*l*-acid (anhydrous acid salt).

The pure malate (mol. wt. 255) is decomposed by warming with very slightly more (Note 5) than two equivalents of approximately 2 *N* sodium hydroxide. The amine is extracted, after cooling, with three or four 25-cc. portions of pure benzene, the solution is dried thoroughly with powdered sodium hydroxide, and the pure amine, b.p., 184–185°, $[\alpha]^{25°}_{D}$ + 39.2° to +39.7° (without solvent), is obtained by distillation (Note 6). A small amount of the amine distils with the benzene. The yield is 35–40 g. (92–94 per cent of the theoretical amount based on the pure malate).

The mother liquors from the original crystallization and recrystallizations are treated in a similar manner and the sodium malate solutions are united and reserved for the recovery of *l*-malic acid (Note 7). The recovered amine amounts to 75–80 g. and contains 40–50 per cent excess *l*-amine.

l-α-Phenylethylamine.—The recovered amine is converted to the acid tartrate in water solution, using for each gram of amine 1.25 g. of *d*-tartaric acid and 4.0 cc. of water. The solution is boiled with decolorizing carbon, if necessary, filtered, and allowed to cool slowly without disturbance (Note 3). A dense mass of coarse crystals of crude *l*-α-phenylethylamine-*d*-tartrate is deposited. The solution is decanted and evaporated to about two-thirds its original volume, and a second crop of crystals is obtained as before. These operations are repeated once or twice more, after which usually no more coarse crystals, but only a mass of needle-like crystals (mixed salts), can be obtained (Note 8). Meanwhile the first crop is recrystallized from about twice its weight of water. About two-thirds of the weight of crude salt is thus obtained pure; the mother liquor is used as solvent for the second crop, and so forth. The final mother liquor is united with that from the original crystallization and reserved for the recovery of the partially resolved amine. The yield of pure *l*-base-*d*-acid salt (anhydrous acid salt) is 75–100 g., an amount equivalent to somewhat more than the excess of

l-amine in the mixture taken. The pure salt has a specific rotation of +13.0 to 13.2° in an 8 per cent solution in water.

The pure salt (mol. wt. 271) is dissolved in four parts of water; the amine is liberated with an excess of 20–25 per cent sodium hydroxide solution, extracted with benzene, and purified as described for the *d*-amine. The constants agree closely with those given for the *d*-amine, and the yield is 32–42 g. (94–96 per cent of the theoretical amount based on the pure tartrate or 53–70 per cent based on the total *l*-amine originally present).

The amine recovered in the same way from the mother liquors amounts to 40–50 g. and contains a slight excess of *d*-amine. It may be used conveniently in the next run in place of the *dl*-amine.

2. Notes

1. The amount of malic acid theoretically is sufficient to convert half of the amine to the acid salt and the remaining half to the neutral salt.

2. Small amounts of the volatile amine are lost by hydrolysis during the evaporation and recrystallization of the salt.

3. Fractional crystallization is facilitated by inoculating the warm solution with a crystal of the species expected to separate and allowing crystallization to proceed slowly without disturbance.

4. The purity of *d*-α-phenylethylamine-*l*-malate is not readily determined by its melting point or specific rotation, but rather by its massive crystalline form and solubility. The acid and neutral *l*-base-*l*-acid salts are much more soluble, and usually do not crystallize at all.

5. Excess alkali must be avoided if the malic acid is to be recovered, since it is slowly racemized by heating with concentrated alkali.

6. When the amine is to be us d in water solution a weighed amount of the pure salt may be decomposed with alkali, the base distilled quantitatively with steam, and the entire distillate used.

7. The solution containing sodium malate is neutralized with acetic acid, diluted to contain about 5 per cent of sodium

malate, and treated at the boiling point with 10 per cent lead acetate solution until lead malate no longer precipitates. The lead malate is collected after cooling and washed by trituration with boiling water. The salt is made into a thin paste with distilled water and decomposed with hydrogen sulfide (two days). The lead sulfide is filtered and the malic acid solution evaporated to a convenient volume. After titration of an aliquot, the solution may be used instead of pure acid in another run. The recovery is 70–80 per cent.

8. The *l*-base-*d*-acid salt no longer can be obtained pure when the solution contains about equal proportions of the salts of *d*- and *l*-amines. For this reason, also, an initial resolution of the *dl*-amine with *d*-tartaric acid is not feasible.

3. Methods of Preparation

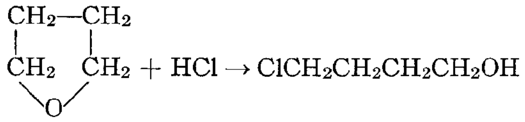
The present method is adapted from that of Lovén.[1] The resolution has been carried out with *d*-α-bromocamphor-π-sulfonic acid (*l*-form);[2,3] with *l*-and *dl*-malic acids (*d*- and *l*-forms);[4] with *l*-quinic acid and *d*-tartaric acid (*d*- and *l*-forms),[5] and with *d*- and *l*-6,6′-dinitrodiphenic acids (*d*- and *l*-forms).[6] Methods employing *d*-benzylmethylacetyl chloride,[7] *d*-oxymethylenecamphor,[8] *l*-quinic acid,[9] and *d*-camphoric anhydride [10] are of theoretical interest only. The *dl*-amine is not resolved by the active camphor-10-sulfonic acids [11] or mandelic acids.[12]

[1] Lovén, J. prakt. Chem. **72**, (2) 307 (1905). See also Lovén, Ber. **29**, 2313 (1896).
[2] Hunter and Kipping, J. Chem. Soc. **83**, 1147 (1903).
[3] Ingold and Wilson, ibid. 1502 (1933).
[4] Ingersoll, J. Am. Chem. Soc. **47**, 1168 (1925).
[5] André and Vernier, Compt. rend. **193**, 1192 (1931).
[6] Ingersoll and Little, J. Am. Chem. Soc. **56**, 2123 (1934).
[7] Kipping and Salway, J. Chem. Soc. **85**, 444 (1904).
[8] Pope and Read, ibid. **95**, 171 (1909).
[9] Marckwald and Meth, Ber. **38**, 801 (1905).
[10] Freylon, Ann. chim. phys. (8) **15**, 140 (1908).
[11] Pope and Harvey, J. Chem. Soc. **75**, 1110 (1899).
[12] Ingersoll, Babcock and Burns, J. Am. Chem. Soc. **55**, 411 (1933).

XXVIII

TETRAMETHYLENE CHLOROHYDRIN

(4-Chlorobutanol-1)



Submitted by DONALD STARR and R. M. HIXON.
Checked by JOHN R. JOHNSON and H. B. STEVENSON.

1. Procedure

A 500-cc. three-necked flask containing 114 g. (1.58 moles) of tetrahydrofuran (Org. Syn. **16**, 77) is fitted with a reflux condenser, a thermometer dipping into the liquid, and a bent glass tube arranged to introduce gaseous hydrogen chloride (Note 1) near the bottom of the flask. The upper end of the reflux condenser is connected to a 150-cc. distilling flask cooled in an ice-salt mixture to trap material entrained by the hydrogen chloride.

The tetrahydrofuran is heated to the boiling point (64–65°), and a slow stream of hydrogen chloride is bubbled into the liquid. As the reaction proceeds the temperature of the boiling liquid increases slowly at first, and then more rapidly until it is above 100° (after about four hours' heating). At the end of about five hours the temperature remains practically constant in the range 103.5–105.5°, and the reaction is stopped. The light brown liquid is cooled, transferred to a 250-cc. Claisen flask having a 20-cm. fractionating side arm, and fractionated at reduced pressure, using a water aspirator. A large quantity of hydrogen chloride is evolved at the start of the distillation and a low pressure cannot be obtained until this has been removed. Throughout the fractionation a trap cooled to −15° in an ice-salt mixture is used to collect the recovered tetrahydrofuran.

After removal of a small amount of low-boiling material the main fraction distils in the range 80–90°/14 mm. or 65–75°/7 mm. (Note 2) and weighs 95–100 g. A small amount (5–10 g.) of high-boiling material remains. The crude product on refractionation yields 93–98 g. (54–57 per cent of the theoretical amount) of pure tetramethylene chlorohydrin boiling over a one-degree interval, 81–82°/14 mm. or 70–71°/7 mm. (Notes 3 and 4).

2. Notes

1. Hydrogen chloride prepared by dropping concentrated sulfuric acid into a mixture of sodium chloride and concentrated hydrochloric acid may be used directly without drying.

2. It has been reported [1] that tetramethylene chlorohydrin undergoes loss of hydrogen chloride when distilled at pressures appreciably above 15 mm. If an oil pump is used for the distillation of the main fraction, it should be protected from hydrogen chloride by means of soda-lime towers.

3. For recovery of tetrahydrofuran, the condensate from the cooling traps and the low-boiling material from the fractionations are combined, cooled in an ice bath, and treated carefully with 15–20 cc. of 40 per cent alkali. The upper layer is separated, dried with a little calcium chloride, and distilled. The recovered tetrahydrofuran, b.p. 64–67°, weighs 20–22 g. (17–19 per cent of the original material). The residue (12–14 g.) remaining after distillation of the tetrahydrofuran distils at 43–45°/10 mm. and is tetramethylene dichloride.

4. Tetramethylene chlorohydrin may be converted to the chlorobromide in excellent yields by the action of phosphorus tribromide.[2]

3. Methods of Preparation

Tetramethylene chlorohydrin was first prepared in a pure state by the action of thionyl chloride on tetramethylene glycol in the presence of pyridine.[1] The method given here has been published recently.[2]

[1] Kirner and Richter, J. Am. Chem. Soc. **51**, 2503 (1929).
[2] Starr and Hixon, ibid. **56**, 1595 (1934).

XXIX

TRICARBETHOXYMETHANE

(Ethyl Methanetricarboxylate)

$$CH_2(CO_2C_2H_5)_2 + Mg + C_2H_5OH \rightarrow C_2H_5OMgCH(CO_2C_2H_5)_2 + H_2$$

$$C_2H_5OMgCH(CO_2C_2H_5)_2 + ClCO_2C_2H_5 \rightarrow ClMgC(CO_2C_2H_5)_3 + C_2H_5OH$$

$$ClMgC(CO_2C_2H_5)_3 + CH_3CO_2H \rightarrow CH(CO_2C_2H_5)_3 + CH_3CO_2MgC$$

Submitted by HAKON LUND and AXEL VOIGT.
Checked by WALLACE H. CAROTHERS and W. L. MCEWEN.

1. Procedure

IN a 1-l. round-bottomed flask provided with an efficient and not too narrow reflux condenser are placed 25 g. (1.03 gram atoms) of magnesium turnings (Grignard), 25 cc. of absolute alcohol (Note 1), 1 cc. of carbon tetrachloride (Note 2), and 30 cc. of a mixture of 160 g. (151 cc., 1 mole) of ethyl malonate and 80 cc. of absolute alcohol. Provision is made for cooling the flask when necessary in cold water, and the mixture is gently heated until hydrogen is evolved. The reaction may become so violent that external cooling is necessary. The ethyl malonate is gradually added through the condenser, care being taken that the reaction proceeds vigorously but not beyond control. When the reaction moderates the flask is cooled and 300 cc. of ether, dried twenty-four hours with calcium chloride, is added through the condenser. On gentle heating the crystals which have separated are dissolved and hydrogen is again evolved for some time without heating. The reaction is brought to completion on the steam bath. The flask is then removed from the steam bath and a

mixture of 100 cc. of ethyl chloroformate (1.05 moles) and 100 cc. of dry ether is added through the condenser from a dropping funnel at such a rate that vigorous boiling is maintained throughout the addition (Note 3). The reaction is complete after heating for fifteen minutes on the steam bath.

The viscous magnesium compound formed is cautiously decomposed with dilute acetic acid (75 cc. in 300 cc. of water), the flask being cooled under the tap. Two clear layers are formed, and after separation, the aqueous layer is extracted with 100 cc. of ether, the combined ethereal solution is washed with water and dried with sodium sulfate, and the ether is distilled on the steam bath. The residue is distilled under reduced pressure. After a small fore-run the temperature rapidly rises to 130° at 10 mm. when the pure tricarbethoxymethane begins to distil. The yield of material collected over a five-degree interval is 204–215 g. (88–93 per cent of the theoretical amount). The product solidifies at 25°. The melting point of the pure substance is 28–29°.

2. Notes

1. Anhydrous alcohol is preferable, but a good grade of commercial absolute alcohol may be used without appreciably lowering the yield. The authors used alcohol dehydrated by means of magnesium.[1]

2. Carbon tetrachloride (as well as a number of other halogen compounds) greatly accelerates the reaction between magnesium and alcohol. If anhydrous alcohol is used the reaction will start in the course of some time without heating, whereas 99.5 per cent alcohol has to be heated nearly to the boiling point before the evolution of hydrogen becomes rapid.

3. Towards the end of the reaction the magnesium compound of ethyl methanetricarboxylate separates as a viscous mass which tends to prevent the remaining magnesium malonic ester and the chloroformate from reacting. Vigorous boiling keeps the material from forming a compact mass. If larger runs are made it may be necessary to apply stirring during this part of the process.

3. Methods of Preparation

Tricarbethoxymethane has been prepared by the action of ethyl chloroformate upon sodiomalonic ester in benzene suspension [2] and by distillation of ethyl ethoxalylmalonate.[3] The present method has been described briefly by one of the authors.[4] It is simpler and gives better yields than the method described in Org. Syn. **13**, 100, for the preparation of the corresponding methyl ester.

[1] Lund and Bjerrum, Ber. **64**, 210 (1931).
[2] Conrad and Guthzeit, Ann. **214**, 32 (1882).
[3] Bouveault, Bull. soc. chim. [3] **19**, 79 (1898); Scholl and Egerer, Ann. **397**, 353 (1913).
[4] Lund, Ber. **67**, 938 (1934).

XXX

TRIPHENYLETHYLENE

$$C_6H_5CH_2MgCl + (C_6H_5)_2CO \rightarrow (C_6H_5)_2C(OMgCl)CH_2C_6H_5$$

$$(C_6H_5)_2C(OMgCl)CH_2C_6H_5 + H_2O \rightarrow (C_6H_5)_2C(OH)CH_2C_6H_5 + Mg(OH)Cl$$

$$(C_6H_5)_2C(OH)CH_2C_6H_5 \xrightarrow{(H_2SO_4)} (C_6H_5)_2C{=}CHC_6H_5 + H_2O$$

Submitted by Homer Adkins and Walter Zartman.
Checked by C. R. Noller and F. M. McMillan.

1. Procedure

In a 3-l. three-necked flask, fitted with a mechanical stirrer, a reflux condenser, and a separatory funnel, are placed 24.3 g. (1 gram atom) of magnesium turnings, 500 cc. of absolute ether, a crystal of iodine, and a 5- to 10-cc. portion of 126.5 g. (114 cc., 1 mole) of freshly distilled benzyl chloride (b.p. 177–179°). In a few minutes the reaction starts (Note 1) and is controlled if necessary by cooling with a wet towel. The stirrer is started and the balance of the benzyl chloride is run in as fast as the refluxing will permit. The addition requires from one to two hours, and when completed the mixture is refluxed on the steam bath with stirring for three hours. With the stirrer still running, 182 g. (1 mole) of benzophenone (Org. Syn. Coll. Vol. 1, 89) dissolved in 500 cc. of absolute ether is added at such a rate that the mixture refluxes rapidly. This requires about twenty minutes and then the reaction mixture is allowed to stand for two hours (Note 2).

The flask is placed in an ice bath, 700 g. of cracked ice is added, and the magnesium hydroxide is dissolved by adding 500 cc. of cold 20 per cent sulfuric acid. The ether layer is separated, and the water layer extracted with two 200-cc. por-

tions of ether. The ether is distilled from the combined extracts, and the residual liquid is refluxed for two hours with 100 cc. of 20 per cent sulfuric acid to dehydrate the carbinol. The layers are separated and the product vacuum-distilled (Note 3). The fraction boiling at 215–225°/15 mm. weighs 160–170 g. and melts at 60–68° (Note 4). Crystallization from 900 cc. of hot 95 per cent alcohol and cooling to 0° gives 140–150 g. of the hydrocarbon melting at 68–69° (54–59 per cent of the theoretical amount). Concentration of the mother liquor to 150 cc. and cooling gives 5–10 g., m.p. 65–67.5° (Note 5).

2. Notes

1. If the reaction does not start within thirty minutes, the mixture is warmed on a water bath with the stirrer running.
2. Slightly better yields are obtained if the reaction mixture is allowed to stand overnight.
3. The product should not be washed with water as the presence of a trace of sulfuric acid during the distillation seems to be necessary to complete the dehydration.
4. Seeding is usually necessary to induce crystallization.
5. Using the same procedure, stilbene may be prepared from benzaldehyde and benzylmagnesium chloride in 25–35 per cent yield.

3. Methods of Preparation

Triphenylethylene has been prepared by the reaction of phenylmagnesium bromide with benzyl benzoate,[1] with desoxybenzoin,[2] or with ethyl phenylacetate,[2] and by the reaction of diphenylketene-quinoline with benzaldehyde.[3] The above procedure is an adaptation of that described by Hell and Wiegandt.[4]

[1] Stadnikoff, Ber. **47**, 2140 (1914).
[2] Klages and Heilmann, ibid. **37**, 1455 (1904).
[3] Staudinger and Kon, Ann. **384**, 89 (1911).
[4] Hell and Wiegandt, Ber. **37**, 1429 (1904).

APPENDIX

LATER REFERENCES TO PREPARATIONS IN THE PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have been described recently. The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses.)

Acrolein Acetal (**11**, 1): By treating acrolein with ethyl orthoformate in the presence of ammonium nitrate. Fischer and Baer, Helv. Chim. Acta **18**, 514 (1935).

Adipic Acid (Coll. Vol. **1**, 18): By the catalytic oxidation of cyclohexanone. Brit. pat. 415,172 [C. A. **29**, 818 (1935)]; U. S. pat. 2,005,183 [C. A. **29**, 5125 (1935)]; Fr. pat. 44,372 [C. A. **29**, 2975 (1935)].

1-Amino-2-naphthol-4-sulfonic Acid (**11**, 12): An improvement of the original method (see **15**, 91). Fieser and Fieser, J. Am. Chem. Soc. **57**, 491 (1935).

***l*-Arabinose** (Coll. Vol. **1**, 60): A procedure is described by which 14.4 g. of *l*-arabinose can be obtained from 100 g. of gum acacia. Carrington, Haworth, and Hirst, J. Chem. Soc. 1653 (1934).

Benzoin (Coll. Vol. **1**, 88): Illumination with a quartz mercury arc results in a decrease in the yield. Bousset, Bull. soc. chim. (5) **2**, 309 (1935).

***n*-Butyl Bromide** (Coll. Vol. **1**, 26): On the basis of comparative studies it is reported that the hydrobromic-sulfuric acid method gives the best yields (92–95 per cent), the sodium bromide method comes next (75–97 per cent), and the phosphorus tribromide method third (69–83 per cent). Omission of sulfuric acid in using the hydrobromic acid method gives very inferior results. Tseng, Ho, and Chia, Science Quart., Natl. Univ. Peking **5**, 375 (1935) [C. A. **29**, 6568 (1935)].

***n*-Butyl *n*-Butyrate** (Coll. Vol. **1**, 135): By catalytic esterification. Turova, Balandin, Merkurova, and Guseva, J. Applied Chem. (U.S.S.R.) **7**, 1454 (1934) [C. A. **29**, 5814 (1935)].

By passing a mixture of *n*-butyric acid and hydrogen over a catalyst at 280–400°. U. S. pat. 1,997,172 [C. A. **29**, 3686 (1935)].

Desoxybenzoin (**12**, 16): By the alkali fusion of desylthioglycolic acid. Behagel and Schneider, Ber. **68**, 1588 (1935).

Ethyl Ethylenetetracarboxylate (**11**, 36): By the use of moist benzene as the solvent the yield is increased to 80 per cent. Malachowski and Sienkiewiczowa, Ber. **68**, 33 (1935).

From dibromomalonic ester and sodiomalonic ester. Adickes, J. prakt. Chem. (2) **145**, 236 (1936).

Ethyl Pimelate (**11**, 42): By an improved procedure the acid is obtained in 50 per cent yield. Müller, Monatsh. **65**, 18 (1934).

Furan (Coll. Vol. **1**, 269): From furoic acid, by an adaptation of the method of Gilman and Louisinian (using quinoline and copper oxide), in 90 per cent yield (crude). Wagner and Simons, J. Chem. Education **13**, 270 (1936).

Furoic Acid (Coll. Vol. 1, 270): In 80 per cent yield by the oxidation of furfural with alkaline potassium permanganate. Wagner and Simons, J. Chem. Education 13, 270 (1936).

d-**Glutamic Acid** (Coll. Vol. 1, 281): By the hydrolysis of wheat gluten in the presence of copper or ferric chloride. Cheng and Adolph, J. Chinese Chem. Soc. 2, 221 (1934) [C. A. 29, 740 (1935)].

Glutaric Acid (Coll. Vol. 1, 283; 14, 90): By the catalytic oxidation of cyclopentanone with oxygen or air in the liquid phase. U. S. pat. 2,005,183 [C. A. 29, 5125 (1935)].

Glycine Ethyl Ester Hydrochloride (14, 46): From the imidic ester hydrochloride by hydrogenation. Ger. pat. 604,277 [C. A. 29, 812 (1935)].

Guanidine Nitrate (Coll. Vol. 1, 295): From ammonium thiocyanate, lead nitrate, and ammonia at 120°. Gockel, Z. angew. Chem. 48, 430 (1935).

n-**Heptylamine** (11, 58): By the hydrogenation of *n*-heptamide in the presence of copper-chromium oxide catalyst at 250° and a pressure of 200–300 atmospheres. Wojcik and Adkins, J. Am. Chem. Soc. 56, 2419 (1934).

n-**Hexadecane** (15, 27): Methods recommended as rendering the pure hydrocarbon more easily available include the reduction of cetyl iodide (*a*) with zinc dust in acetic acid solution, (*b*) with zinc-copper couple and alcohol, and (*c*) with hydrogen and palladinized calcium carbonate in propyl alcohol solution. Yields of 90–95 per cent are reported. Cary and Smith, J. Chem. Soc. 346 (1933).

Hydrobromic Acid (Coll. Vol. 1, 23): From sodium bromide and dilute sulfuric acid, on distillation. Tseng, Ho, and Chia, Science Quart., Natl. Univ. Peking, 5, 337 (1935) [C. A. 29, 2871 (1935)].

Ketene (Coll. Vol. 1, 325): A convenient and compact ketene generator is described. Herriott, J. Gen. Physiol. 18, 69 (1934).

l-**Menthone** (Coll. Vol. 1, 333): By the sulfochromic oxidation of menthol. Dulow, Bull. inst. pin 173 (1934) [C. A. 29, 2946 (1935)].

Mesitylene (Coll. Vol. 1, 334): Preparation in 43 per cent yield, based on the acetone used, by heating acetone with 5 vol. per cent of concentrated hydrochloric acid at 145° and an initial pressure of 100 atmospheres for twenty-four hours. Ipatiew, Dolgow, and Wolnow, Ber. 63, 3072 (1930). The synthesis can be effected at lower pressures than that first recommended. Sucharda and Kuczyński, Roczniki Chem. 14, 1182 (1934) [C. A. 29, 6214 (1935)].

By the catalytic dehydration of acetone with bauxite at temperatures of 250–450° and under pressures of 50–300 atmospheres. U. S. pat. 1,977,178 [C. A. 29, 181 (1935)].

α-**Naphthoic Acid** (11, 80): Obtained in 85 per cent yield by preparing the Grignard reagent as described and pouring the solution onto solid carbon dioxide. Fieser, Holmes, and Newman, J. Am. Chem. Soc. 58, 1055 (1936).

The ethyl ester has been obtained in 70 per cent yield from the reaction of α-naphthylmagnesium bromide and diethyl carbonate. Loder and Whitmore, J. Am. Chem. Soc. 57, 2727 (1935).

m-**Nitroacetophenone** (10, 74): By varying certain details of the procedure the yield of material melting at 77° was raised to 83 per cent of the theoretical amount. This paper includes a further survey of the literature. Morgan and Watson, J. Soc. Chem. Ind. 55, 29T (1936).

1-Nitro-2-acetylaminonaphthalene (13, 72): Notes concerning the procedure and the preparation of the starting material. Schiemann and Ley, Ber. 69, 963 (1936).

p-**Nitrobenzoyl Chloride** (Coll. Vol. 1, 387): Pyridine is used (in considerable quantity) to catalyze the reaction of the acid, suspended in ether, with thionyl chloride. Carré and Libermann, Compt. rend. 199, 1422 (1934).

n-**Pentane** (11, 84). By the electrolytic reduction of methyl *n*-propyl ketone. Swann and Feldman, Trans. Electrochem. Soc. 67, 6 (1934); Swann, Deditius, and Pyhrr, ibid. 68, 7 (1935).

Phenylglyoxal (15, 67): In 40 per cent yield by the action of alkali on diphenyldithiodiglycolic acid. Schöberl, Berninger, and Harren, Ber. 67, 1545 (1934).

Phthalaldehyde Acid (16, 68): By the photochemical chlorination of phthalide, followed by hydrolysis. U. S. pat. 2,047,946 [C. A. 30, 6011 (1936)].

Platinum Catalyst for Reductions (Coll. Vol. 1, 452): Preparation from platinum black by heating with oxygen under pressure. Laffite and Grandadam, Compt. rend. 200, 456 (1935).

To obtain catalyst of maximum and reproducible activity, it is recommended that the fusion be conducted in a Pyrex beaker or casserole resting in a cavity of a copper block heated with a burner and provided with a thermometer well. Adequate temperature control is thus possible. Short, J. Soc. Chem. Ind. 55, 14T (1936).

Taurine (10, 98): In 40 per cent yield by the oxidation of cystamine. Schöberl, Z. physiol. Chem. 216, 193 (1933).

By an adaptation of Reychler's method, large quantities of β-aminoethyl bromide hydrobromide and taurine are obtained conveniently in yields of 90 and 80 per cent, respectively. Cortese, J. Am. Chem. Soc. 58, 191 (1936).

Tetrahydrofuran (16, 77): By the action of thionyl chloride on tetramethylene glycol. Strukov, Khim. Farm. Prom. 1, 35 (1935) [C. A. 30, 1769 (1936)].

In quantitative yield by the two-stage hydrogenation of furan in the presence of osmium-asbestos catalyst. Shuĭkin and Chilikina, J. Gen. Chem. (U.S.S.R.) 6, 279 (1936) [C. A. 30, 4855 (1936)].

β-**Thiodiglycol** (12, 68): From ethylene oxide and hydrogen sulfide. Chichibabin and Bestuzhev, Compt. rend. 200, 242 (1935); Nenitzescu and Scărlătescu, Ber. 68, 587 (1935).

Thymoquinone (Coll. Vol. 1, 498): By refluxing nitrosothymol with 8 per cent hydrochloric acid for two days and distilling the product with steam, somewhat impure thymoquinone was obtained in 70–77 per cent yield. Tseng, Hu, and Chu, J. Chinese Chem. Soc. 2, 136 (1934) [C. A. 29, 464 (1935)].

ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of the compound refer to the volume and page of Organic Syntheses. New methods or changes in procedure have not been checked unless otherwise noted.)

Azoxybenzene (11, 16):

The reduction of nitrobenzene in alkaline medium is accomplished conveniently using dextrose (*d*-glucose monohydrate). In a 1-l. three-necked flask fitted with a reflux condenser and an efficient stirrer (p. 31) there are placed 60 g. of sodium hydroxide, 200 cc. of water, and 41 g. (34.2 cc., 0.33 mole) of nitrobenzene. The flask is immersed in a water bath kept at 55–60°, and 45 g. (0.23 mole) of dextrose is introduced in portions, with continuous stirring, in the course of one hour. The temperature of the bath is then raised to 100° and kept there for two hours. The hot mixture is poured into a 2-l. long-necked flask and steam-distilled to remove nitrobenzene and aniline. When the distillate is clear (twenty minutes, 2 l. of distillate) the residue is poured into a beaker and cooled well in an ice bath. The azoxybenzene, which solidifies, is collected, the lumps are ground in a mortar, and the product is washed with water and dried. The yield of material melting at 34–35° is 26–27 g. (79–82 per cent of the theoretical amount). Crystallization from 15 cc. of methyl alcohol gives material melting at 35–35.5° with 90 per cent recovery.

Nicholas Opolonick, private communication. Checked by L. F. Fieser and M. Fieser.

β-Chloropropionic Acid (Coll. Vol. **1**, 162):

The yield can be improved materially by controlling the temperature during the oxidation, and the procedure can be

simplified to advantage as follows. A 3-l. long-necked Pyrex flask containing 880 g. (620 cc., 10 moles) of concentrated nitric acid (sp. gr. 1.42) is supported in an ice bath and supplied with a mechanical stirrer and a thermometer suspended into the liquid (hood). While controlling the temperature to 25–30° by suitable cooling, 200 g. (2.12 moles) of trimethylene chlorohydrin is run in from a dropping funnel. The addition takes two to three hours.

The oxidation proceeds rapidly under the catalytic influence of the oxides of nitrogen formed, but there is sometimes difficulty in starting the reaction using pure nitric acid. In this case the checkers found it convenient to oxidize a few drops of the chlorohydrin with nitric acid by heating in a test tube and to add this to the nitric acid in the flask without stirring. A small portion of the chlorohydrin is then added and allowed to react for a few minutes before starting the stirrer and continuing the oxidation of the main lot.

After the chlorohydrin has been added the mixture is stirred for one-half hour longer, allowed to stand overnight, heated for one hour on the steam bath, and distilled as directed. The yield of β-chloropropionic acid boiling at 107–109°/20 mm. and freezing at 39° is 179–181 g. (78–79 per cent of the theoretical amount).

E. H. Huntress and E. B. Hershberg, private communication. Checked by L. F. Fieser and A. M. Seligman.

Coupling of o-Tolidine and Chicago Acid (16, 12):

Two methyl groups were omitted from the formula of the dye.

2,4-Dimethyl-3,5-dicarbethoxypyrrole (15, 17):

It is reported that the yield is increased to 75 per cent by adding sodium acetate to the zinc dust reduction mixture to form a complex with the zinc acetate and so increase its solubility, and by adding the solution of the nitroso compound to the mixture of zinc dust, sodium acetate, ethyl acetoacetate, and glacial acetic acid, instead of adding the zinc dust last.

Corwin and Quattlebaum, Jr., J. Am. Chem. Soc. **58,** 1083 (1936).

γ-Phenylbutyric Acid (15, 64):

By adding toluene to the reaction mixture an equally pure product is obtained in somewhat better yield, polymolecular reactions being inhibited at the high dilution in the aqueous phase. The zinc is amalgamated conveniently by placing 120 g. of mossy zinc, 12 g. of mercuric chloride, 200 cc. of water, and 5–6 cc. of concentrated hydrochloric acid in a 1-l. round-bottomed flask and shaking for five minutes. The solution is decanted and the following reagents are added in order: 75 cc. of water, 175 cc. of concentrated hydrochloric acid, 100 cc. of toluene, and 50 g. (0.28 mole) of β-benzoylpropionic acid. The mixture is boiled briskly under a reflux condenser for twenty-five to thirty hours, adding three 50-cc. portions of concentrated hydrochloric acid at intervals of about six hours. After cooling to room temperature the layers are separated and the aqueous layer is diluted with 200 cc. of water and extracted with three 75-cc. portions of ether. The combined ether-toluene solution is washed with water, dried with calcium chloride, and the solvent is removed by distillation under diminished pressure on the steam bath. The product is obtained by distillation as a colorless solid, b.p. 178–181°/19 mm., m.p. 46–48°. The yield is 38–41 g. (83–90 per cent of the theoretical amount).

In isolating higher-melting compounds prepared by this method (e.g., γ-naphthylbutyric acids), the layers are separated after cooling to 50–60°, benzene is used for the extraction, and the combined solution is clarified with Norite while still wet, concentrated somewhat, and allowed to cool for crystallization. In preparing methoxylated acids such as γ-anisyl- or γ-veratrylbutyric acid some demethylation occurs and a modification is necessary. The toluene layer and extracts are mixed with an excess of dilute sodium hydroxide and the organic solvents are

removed by steam distillation. The alkaline solution is treated at 80° with an excess of dimethyl sulfate, the solution is clarified with Norite, cooled, and acidified, when the product separates in good condition.

E. L. MARTIN, private communication and J. Am. Chem. Soc., 58, 1438 (1936). Checked by C. R. NOLLER and F. M. MCMILLAN.

Platinum Catalyst for Reductions (Coll. Vol. **1**, 452):

Ammonium chloroplatinate often can be used to advantage in place of chloroplatinic acid in the preparation of Adams' catalyst. A mixture of 3 g. of ammonium chloroplatinate and 30 g. of sodium nitrate in a casserole or Pyrex beaker is heated gently at first until the rapid evolution of gas slackens and then more strongly until a temperature of 500° is reached. This operation requires about fifteen minutes and there is no spattering. The temperature is held at 500–520° for one-half hour and the mixture is then allowed to cool. The platinum oxide catalyst, collected in the usual way by extracting the soluble salts with water, weighs 1.5 g. and it is comparable in appearance and in activity to the material prepared from chloroplatinic acid.

This procedure is particularly time-saving when scrap platinum or spent catalyst is used for the preparation of platinum oxide, for after conversion to chloroplatinic acid a purification is conveniently effected by precipitating the ammonium salt, and the direct fusion of this with sodium nitrate eliminates the tedious process of reconversion to chloroplatinic acid. Furthermore ammonium chloroplatinate is not hygroscopic and can be accurately weighed. The amount of catalyst obtained is almost exactly half the weight of the ammonium salt employed.

WILLIAM F. BRUCE, private communication and J. Am. Chem. Soc. 58, 687 (1936). Checked by L. F. FIESER, R. P. JACOBSEN and M. S. NEWMAN.

***o*-Sulfobenzoic Anhydride** (Coll. Vol. **1**, 484):

Reference 6 should read: White and Acree, J. Am Chem· Soc. 41, 1197 (1919).

SUBJECT INDEX

(This Index Comprises Material from Volumes X to XVII of this Series; for Previous Volumes see Collective Volume 1.)

(Names in small capital letters refer to the titles of preparations which are given in full detail. A number in ordinary bold face type denotes the volume. A number in bold face italics refers to a page which gives preparative directions for a substance formed either as principal product or as a by-product, or to a product which has been prepared by a method analogous to the one given. Other numbers in ordinary type indicate pages on which a compound is mentioned incidentally or information is given concerning an item other than a compound.)

Acetal, **10**, 107
Acetaldehyde, **12**, 48
Acetamide, **14**, 84
Acetic acid, purification, **17**, 47
Acetic anhydride, **12**, 1; **13**, 8; **14**, 40; **15**, 85; **16**, 28
ACETO-*p*-CYMENE, **14**, ***1***
ACETOL, **10**, ***1***, 84
Acetone, **10**, 12; **11**, 4; **12**, 22; **15**, 1; **17**, 41
ACETONE CYANOHYDRIN, **11**, ***4***; **15**, ***1***
Acetonitrile, **15**, 70
Acetonylacetone, **16**, 25, ***26***
o-Acetophenol, **13**, ***92***
p-Acetophenol, **13**, ***92***
Acetophenone, **10**, 74; **11**, 102; **15**, 67; **17**, 76
Acetyl-*β*-aminonaphthalene, **13**, 72
Acetylation
of benzoin, **12**, 1
of *tert.*-butylbenzene, **14**, 3
of cumene, **14**, 3
ACETYL BENZOIN, **12**, ***1***
Acetyl chloride, **14**, 1
Acid chloride, preparation, **12**, 16; **13**, 32; **15**, 77
ACONITIC ACID, **17**, ***1***
Acrolein, **10**, 107; **11**, 26
ACROLEIN ACETAL, **11**, ***1***, 52; **17**, 91
Acyloins, preparation, **13**, 24
Addition of bromine
to cinnamic ester, **12**, 36
to cyclohexene, **12**, 26
Adipic acid, **13**, 32, 106, ***110***; **15**, 87; **17**, 91
Adipyl chloride, **13**, 32
β-ALANINE, **16**, ***1***
dl-Alanine, **10**, 107; **15**, 87
Alcohols, preparation
by Grignard synthesis, **11**, 98; **12**, 48; **15**, 11
by reduction of aldehydes, **15**, 80
by reduction of esters, **10**, 62; **14**, 20; **15**, 51
by reduction of ketones, **10**, 60
Alcoholysis of olive oil, **15**, 52
Alkyl bromides, preparation, **15**, 24
Alkylhydrazines, preparation, **16**, 18, 22, 51
Alkyl iodides, preparation, **13**, 60; **15**, 29
Alkyl nitrites, preparation, **10**, 22; **16**, 7, 44
Alkyl phosphates, preparation, **16**, 9
Alkyl sulfides, preparation, **15**, 72
ALLANTOIN, **13**, ***1***
Allyl alcohol, **10**, 107; **16**, 85
Allyl cyanide, **16**, 85
Alumina, **17**, 27
Aluminum, amalgamated, **14**, 34
Aluminum chloride, **12**, 16, 62, 80; **13**, 12, 32, 90; **14**, 1, 36; **15**, 77; **16**, 45; **17**, 51, 58
Aluminum ethoxide, **15**, ***82***
Aluminum ethylate, **15**, ***82***
Amides, preparation from nitriles, **13**, 95; **16**, 4

Amines, preparation from ketones, **17**, 76
m-Aminobenzaldehyde, **13**, 28
o-Aminobenzenesulfonic acid, **15**, *55*
p-Aminobenzoic acid, **13**, 54
γ-Aminobutyric acid, **17**, *4*
α-Amino-*iso*-butyric acid, **11**, *4*
ε-Aminocaproic acid, **17**, *7*
2-Aminoethanesulfonic acid, **10**, *98*
2-Aminofluorene, **13**, *74*
1-Amino-2-naphthol hydrochloride, **11**, *8*; **17**, *9*, 68
1-Amino-4-naphthol hydrochloride, **17**, *9*, 69
1-Amino-2-naphthol-4-sulfonic acid, **11**, *12*; **15**, 91; **17**, 91
Aminonaphtholsulfonic acids, coupling to form azo dyes, **16**, 16
p-Aminophenol, **15**, 39
Aminopiperole, **16**, 6
β-Aminopropionic acid, **16**, *1*
4-Aminoveratrole, **16**, *4*
Ammonium dichromate, **15**, 74
Ammonium formate, **17**, *78*
Ammonium thiocyanate, **15**, 74
Ammonium vanadate, **13**, 110
n-Amyl alcohol, **13**, 17
tert.-Amyl alcohol, **13**, 68
n-Amylbenzene, **10**, *4*
n-Amyl borate, **13**, *17*
n-Amyl bromide, **16**, 41
iso-Amyl iodide, **13**, *62*
n-Amyl iodide, **13**, *62*
n-Amylmagnesium bromide, **16**, 41
iso-Amyl nitrite, **16**, *8*
n-Amyl phosphate, **16**, *10*
sec.-Amyl sulfide, **15**, *73*
Aniline, **11**, 62; **13**, 96; **14**, 24; **15**, 59
Aniline hydrochloride, **13**, 46
Aniline-*o*-sulfonic acid, **15**, *55*
Anisalacetone, **10**, *115*
γ-Anisylbutyric acid, **17**, *97*
Anthracene, **16**, 74
Anthranilic acid, **12**, 76; **17**, 16
Anthraquinone, **14**, 4; **16**, *74*
Apparatus
  for absorbing hydrogen chloride, **12**, 16; **14**, 2, 72
  for brominating aniline, **13**, 96
Apparatus, (*Continued*)
  for catalytic hydrogenation, **16**, 79; **17**, 45
  for continuous extraction, **10**, 104
  for cracking cyclohexene, **17**, 27
  for esterification, **10**, 49; **11**, 102
  for evaporation under reduced pressure, **12**, 4
  for gas absorption, **12**, 12
  for Gattermann-Koch aldehyde synthesis, **12**, 81
  Hershberg stirrer, **17**, 31
  for inverted suction filtration, **16**, 81
  for making fluoboric acid, **13**, 49, 54
  for nitrosation with methyl nitrite, **16**, 44
  for oxidation with oxides of nitrogen, **10**, 54
  for preparation of alkyl iodides, **13**, 60
  for preparation of anhydrous hydrogen bromide, **15**, 35
  for preparation of ethyl nitrite, **10**, 23
  for preparation of ketones with thoria catalyst, **16**, 47
  for steam distillation, **17**, 21
  suction filtration with "rubber dam," **12**, 31
l-Arabinose, **17**, 91
Arginine dinitronaphtholsulfonate, **12**, *5*
d-Arginine hydrochloride, **12**, *4*
Arsanilic acid, **16**, 85
Arsonoacetic acid, **10**, 108
Arylarsonic acid, preparation, **15**, 59
Arylsulfur chlorides, preparation, **15**, 45
Azelaic acid, **13**, *4*; **15**, 87
Azeotropic mixtures, **10**, 89; **13**, 16
Azibenzil, **15**, *62*
Azlactone of α-benzoylamino-β-(3,4-dimethoxyphenyl)-acrylic acid, **13**, *8*; **15**, 31
Azlactone of α-benzoylaminocinnamic acid, **14**, *80*
Azo dyes, preparation and purification, **16**, 12
Azoxybenzene, **11**, *16*; **17**, *95*

Barbituric acid, **12**, 58
Benzalacetophenone, **10**, 80; **14**, 84; **17**, 51
Benzalazine, **16**, *51*
Benzaldehyde, **12**, 5, 6, 22; **16**, 51
Benzalphthalide, **13**, *10*
Benzanthrone, **14**, *4*; **15**, 87, 92; **16**, 85
Benzenediazonium fluoborate, **13**, *47*
p-Benzenediazonium sulfonate, **17**, 9
Benzenesulfonyl chloride, **10**, *6*; **14**, 84
Benzidine dyes, **16**, 16
Benzil, **10**, 108; **15**, 63; **16**, 85
Benzil hydrazone, **15**, *62*
Benzohydrol, **16**, 85
Benzoic anhydride, **15**, 87
Benzoin, **10**, 108; **12**, 1, 20, 34; **17**, 91
Benzophenone, **10**, 10, 28, 108; **11**, 95; **14**, 8; **16**, 85; **17**, 89
Benzophenone dichloride, **11**, 94, *95*
Benzophenoneoxime, **10**, *10*, 28
Benzopinacol, **14**, *8*, 12
β-Benzopinacolone, **14**, *12*
Benzoquinone, **16**, *73*
α-Benzoylaminocinnamic acid, azlactone of, **14**, *80*
α-Benzoylamino-β-(3,4-dimethoxyphenyl)-acrylic acid, azlactone of, **13**, *8*; **15**, 31
Benzoylation, **12**, 41; **16**, 18
γ-Benzoylbutyric acid, **13**, *13*
Benzoyl chloride, **12**, 41, 62; **16**, 18
Benzoylene urea, **17**, *16*
Benzoylformic acid, **16**, *89*
Benzoyl peroxide, **13**, 86
  analysis of, **13**, 88
β-Benzoylpropionic acid, **13**, *12*; **15**, 64, 92; **16**, 85; **17**, 97
Benzyl benzoate, **10**, 108
Benzyl chloride, **12**, 10
Benzyl cyanide, **11**, 40; **16**, 85
  purification, **16**, 89
Benzylidenearginine, **12**, *4*
Benzylmagnesium chloride, **10**, 4
Benzyl phthalimide, **12**, *10*
Biacetyl monoxime, **10**, *22*
Bistyryl, **16**, *28*
Boric acid, **13**, 16, 46, 52
Bromal, **17**, *18*
Bromination
  of acetone, **10**, 12
  of *tert.*-amyl alcohol, **13**, 68
  of aniline, **13**, 96
  of *p*-bromotoluene **17**, 20
  of dibenzoylmethane, **13**, 38
  of 2,4-dihydroxybenzoic acid, **17**, 23
  of mesitylene, **11**, 24
  of naphthalene, **10**, 14
  of *p*-nitrophenol, **15**, 6
  of *p*-nitrotoluene, **16**, 54
  of paraldehyde, **17**, 18
  of pentaerythritol, **17**, 73
  of phenoldisulfonic acid, **14**, 15
  of *iso*-propylmalonic acid, **11**, 20
Bromine, addition, **12**, 26, 36
Bromoacetaldehyde, **17**, 18
Bromoacetone, **10**, 1, *12*; **14**, 84
p-Bromobenzal bromide, **17**, 21
m-Bromobenzaldehyde, **13**, *30*
p-Bromobenzaldehyde, **17**, *20*
p-Bromobenzoic acid, **17**, 21
α-Bromo-*iso*-caproic acid, **11**, *22*
α-Bromo-*n*-caproic acid, **11**, *22*
Bromocyanogen, **11**, *30*
p-Bromodiphenyl, **16**, 85
Bromomesitylene, **11**, *24*, 66
α-Bromo-β-methylvaleric acid, **11**, *22*
α-Bromonaphthalene, **10**, *14*; **11**, 80
m-Bromonitrobenzene, **14**, 67
2-Bromopentane, **11**, 84, *85*
o-Bromophenol, **14**, *14*; **15**, 88
α-*p*-Bromophenylethylamine, **17**, *78*
4-Bromoresorcinol, **17**, *23*
p-Bromotoluene, **17**, 20
α-Bromo-*iso*-valeric acid, **11**, *20*
Buffers, **10**, 18
1,3-Butadiene, **17**, *25*
iso-Butyl alcohol, **13**, 20
n-Butyl alcohol, **10**, 101, 104; **13**, 16; **15**, 51; **16**, 7, 9, 60
n-Butylamine, **11**, *59*
sec.-Butylamine, **11**, *59*
n-Butyl borate, **13**, *16*
iso-Butyl bromide, **13**, *20*; **14**, 84; **16**, 85
n-Butyl bromide, **15**, 11; **17**, 91
sec.-Butyl bromide, **11**, 77; **13**, *21*

n-Butyl *n*-butyrate, **10**, 109; **17**, 91
n-Butyl chloride, **10**, 5, 109
n-Butyl ether, **11**, 84
iso-Butyl iodide, **13**, *62*
n-Butyl iodide, **13**, *62*
sec.-Butyl iodide, **13**, *62*
n-Butyl nitrite, **16**, *7*, 46
n-Butyl oleate, **15**, 51, *52*
n-Butyl phosphate, **16**, *9*
sec.-Butyl phosphate, **16**, *10*
n-Butyl sulfide, **15**, *73*
n-Butyl *p*-toluenesulfonate, **10**, 4; **15**, 88
Butyroin, **13**, *24*
iso-Butyroin, **13**, *26*
o-Butyrophenol, **13**, *92*
p-Butyrophenol, **13**, *92*
n-Butyryl chloride, **14**, *90*; **16**, 86

n-Caproic acid, **11**, *78*; **16**, *62*
ε-Caprolactam, **17**, *60*
o-Caprophenol, **13**, *92*
p-Caprophenol, **13**, *92*
p-Carbethoxybenzenediazonium fluoborate, **13**, *53*
2-Carbethoxycyclopentanone, **17**, *30*
Carbon bisulfide, **12**, 62; **13**, 90
Carbon monoxide, **12**, 80
Carbon tetrachloride, **17**, 86, 87
Casein, **10**, *16*, 100
Castor oil, **13**, 4
Catalyst
  carbon tetrachloride, **17**, 87
  for chlorate oxidations, **11**, 47; **16**, 73
  for zinc reductions, **16**, 71
  Gilman's, for starting Grignard reactions, **11**, 67
  palladous oxide—palladium black, **16**, 77
  platinum, **17**, 93, *98*
  sulfur, **17**, 18
  thorium oxide on pumice, **16**, 49
Catechol, **10**, 109
Cellobiose, **17**, *34*
α-Cellobiose octaacetate, **17**, 34, *36*
Cetyl alcohol, **10**, *64*; **15**, 29
Cetyl iodide, **15**, 27, *29*
Chelidonic acid, **17**, *40*
Chicago acid, **16**, 13
Chloral, **15**, 80
Chlorination of *p*-chlorotoluene, **12**, 12
Chlorine, **12**, 12; **15**, 45; **16**, *5*
Chloroacetic acid, **12**, 40; **13**, 42
m-Chlorobenzaldehyde, **13**, *28*
p-Chlorobenzaldehyde, **12**, *12*
o-Chlorobenzoic acid, **10**, *20*; **14**, 85
o-Chlorobenzoyl chloride, **16**, 86
4-Chlorobutanol-1, **17**, *84*
γ-Chlorobutyronitrile, **13**, 106; **17**, 4
β-Chloroethyl methyl sulfide, **14**, *18*
Chloroform, **17**, 58
p-Chloromercuribenzoic acid, **14**, 85
Chloromethyl ether, **14**, 92
m-Chloronitrobenzene, **14**, 67
α-*p*-Chlorophenylethylamine, **17**, *78*
β-Chloropropionaldehyde acetal, **11**, 1, *26*
β-Chloropropionic acid, **17**, *95*
Chlorosulfonic acid, **10**, 6
o-Chlorotoluene, **10**, 20, 109; **14**, 85
p-Chlorotoluene, **12**, 12
β-Cholestanol, **17**, *45*
Cholestanone, **17**, *43*
Cholesterol, **17**, 45
Cholesteryl acetate, **17**, 45, *47*
Cinnamic aldehyde, **16**, 28
Cinnamyl alcohol, **15**, *84*
Citraconic acid, **11**, *28*, 71, 74
Citraconic anhydride, **11**, *28*, 71, 74
Citric acid, **11**, 70; **13**, 111; **17**, 1
Claisen-Schmidt condensation, **12**, 22
Clemmensen reduction, **17**, 97
Condensation
  of an α,β-unsaturated ketone and ethyl malonate, **15**, 14
  of an aldehyde and an amino acid, **12**, 4
  of an aldehyde and hippuric acid, **13**, 8; **14**, 81
  of benzaldehyde and acetone, **12**, 22
  of benzaldehyde and hydrazine, **16**, 61
  of benzoin and urea, **12**, 34
  of cinnamic aldehyde and phenylacetic acid, **16**, 28
  of a 1,4-diketone and ammonia, **16**, 25
  of an ester to form an acyloin, **13**, 24

Condensation, (*Continued*)
  of ethyl acetoacetate and ethyl α-aminoacetoacetate, **15**, 17
  of ethyl acetoacetate with formaldehyde and ammonia, **14**, 30
  of ethyl acetoacetate with urea, **17**, 63
  of ethyl bromomalonate with itself, **11**, 36
  of ethyl oxalate with acetone, **17**, 40
  of ethyl oxalate and benzyl cyanide, **11**, 40
  of ethyl oxalate with ethyl propionate, **17**, 54
  of ethyl oxalate and phenylacetate, **16**, 33
  of a nitroso compound and dinitrotoluene, **12**, 30
  of phthalic anhydride and phenylacetic acid, **13**, 10
Copper powder, **12**, 46, 55; **14**, 4, *67*
Cotton, **17**, 36
Coupling of *o*-tolidine and Chicago acid, **16**, 12; **17**, 96
Crotyl alcohol, **15**, *84*
Cupferron, **10**, 110
Cuprous bromide, **13**, 30
Cuprous chloride, **12**, 80; **13**, 29
Cyanoacetamide, **10**, 66
Cyanogen bromide, **11**, *30*
Cyanohydrin formation, **15**, 1
Cyclohexanol, **13**, 110; **17**, 27
Cyclohexanoneoxime, **11**, *56*, 59; **17**, 60
Cyclohexene, **12**, 26; **14**, 85; **16**, 86; **17**, 25, *27*
Cyclohexylamine, **11**, *59*
Cyclohexyl bromide, **15**, *26*
Cyclopentanone, **10**, 110; **13**, 110; **14**, 90
p-Cymene, **14**, 1
l-Cystine, **10**, 110

Decamethylene glycol, **14**, *20*
Decarboxylation, **14**, 32; **15**, 20; **17**, 23
Dehydration, **10**, 66, 78; **12**, 66; **13**, 39; **15**, 85, 93; **16**, 75; **17**, 1, 27, 89
Dennis bar, **17**, 3
Desoxybenzoin, **12**, *16*; **13**, 106; **14**, 85; **17**, 91
Desyl chloride, **12**, *20*
Diacetonamine hydrogen oxalate, **14**, 85
Diacetone alcohol, **10**, 110
Diacetyl monoxime, **10**, *22*
Diallylcyanamide, **10**, 110
Diaminodurene, **10**, *41*
2,4-Diamino-1-naphthol, **17**, 13
2,4-Diaminotoluene, **11**, *32*
Dianisalacetone, **10**, *115*
Dianisidine, **16**, 16
Diazoaminobenzene, **14**, *24*
Diazo compounds, aliphatic, preparation, **15**, 3, 62; **16**, 86
Diazofluorene, **15**, 63
Diazomethane, **15**, *3*; **16**, 86
Diazotization
  of *m*-aminobenzaldehyde, **13**, 28
  of *p*-aminophenol, **15**, 39
  of aniline, **13**, 46; **14**, 24; **15**, 59
  of anthranilic acid, **12**, 76
  of benzidine types, **16**, 12
  of ethyl *p*-aminobenzoate, **13**, 52
  of sulfanilic acid, **17**, 9
  of *o*-tolidine, **16**, 12
  of tribromoaniline, **13**, 96
Dibenzalacetone, **12**, *22*
Dibenzohydryldisulfide, **11**, *95*
1,4-Dibenzoylbutane, **13**, *32*
Dibenzoyldibromomethane, **13**, *38*
Dibenzoyldimethylhydrazine, **16**, *19*
Dibenzoylhydrazine, **16**, *18*
Dibenzoylmethane, **13**, 38
Dibenzyl ketone, **16**, *48*
Dibromoacetaldehyde, **17**, 18
2,6-Dibromo-4-aminophenol chlorostannate, **15**, *8*
1,2-Dibromocyclohexane, **12**, *26*
α,γ-Dibromohydrin, **14**, *42*; **16**, 31
Dibromonaphthalene, **10**, 14
2,6-Dibromo-4-nitrophenol, **15**, *6*, 8
2,6-Dibromoquinone-4-chloroimide, **15**, *8*
Di-*n*-butyl carbinol, **15**, *11*
α,γ-Dichlorohydrin, **16**, 30
Diethylamine, **10**, 58; **14**, 28
β-Diethylaminoethyl alcohol, **14**, *28*
Diethyl carbonate, **11**, 98
Diethylzinc, **12**, *86*; **16**, 86

DIHYDROCHOLESTEROL, 17, 43, 45
1,4-Dihydro-3,5-dicarbethoxy-2, 6-dimethylpyridine, 14, 31
2,4-Dihydroxybenzoic acid, 17, 23
2,4-Dihydroxy-5-bromobenzoic acid, 17, 23
2,4-Dihydroxy-3,5-dibromobenzoic acid, 17, 24
2,6-DIIODO-*p*-NITROANILINE, 12, 28
α-Diketones, 15, 68
DIMEDONE, 15, 14
3,4-DIMETHOXYANILINE, 16, 4
3,4-DIMETHOXYBENZALDEHYDE, 13, 8, 102; 15, 85; 16, 88, 91
3,4-DIMETHOXYBENZONITRILE, 15, 85; 16, 4, 92
3,4-DIMETHOXYPHENYLACETIC ACID, 15, 31
3,4-Dimethoxyphenylpyruvic acid, 15, 33
Dimethylamine, nitrosation, 16, 22
p-Dimethylaminobenzophenone, 14, 86
Dimethylaniline, 12, 30
2,4-DIMETHYL-5-CARBETHOXYPYRROLE, 17, 48
5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE, 15, 14
2,4,-DIMETHYL-3, 5-DICARBETHOXYPYRROLE, 15, 17, 20; 17, 96
5,5-DIMETHYLDIHYDRORESORCINOL, 15, 14
2,5-Dimethylfuran, 16, 26
DIMETHYLGLYOXIME, 10, 22; 13, 106
sym.-DIMETHYLHYDRAZINE DIHYDROCHLORIDE, 16, 18
unsym.-DIMETHYLHYDRAZINE HYDROCHLORIDE, 16, 22
Dimethyl malonate, 13, 100
2,6-DIMETHYLPYRIDINE, 14, 30
2,4-DIMETHYLPYRROLE, 15, 20; 17, 48
2,5-DIMETHYLPYRROLE, 16, 25
Dimethyl sulfate, 11, 67; 12, 52; 13, 56, 102; 15, 41, 48; 16, 19, 51
2,4-DINITROANILINE, 15, 22
2,4-DINITROBENZALDEHYDE, 12, 30
Dinitrobenzylidene-*p*-aminodimethylaniline, 12, 31
2,4-Dinitrochlorobenzene, 13, 36; 15, 22
2,6-Dinitrochlorobenzene, 13, 37
Dinitrodurene, 10, 40
2,4-Dinitro-1-naphthol-7-sulfonic acid, 12, 5
Di-*o*-nitrophenyl disulfide, 15, 45, 55
2,4-DINITROPHENYLHYDRAZINE, 13, 36
2,6-Dinitrophenylhydrazine, 13, 37
2,4-Dinitrophenylsulfur chloride, 15, 46
2,4-Dinitrotoluene, 11, 32; 12, 31
1,4-DIPHENYLBUTADIENE, 16, 28
4,5-DIPHENYLGLYOXALONE, 12, 34
Diphenylketimine hydrochloride, 10, 28
Diphenylmercury, 15, 88
DIPHENYLMETHANE, 14, 34
DIPHENYLMETHANE IMINE HYDROCHLORIDE, 10, 28
β,β-DIPHENYLPROPIOPHENONE, 17, 51
DIPHENYL SULFIDE, 14, 36
DIPHENYL SULFONE, 10, 6
DIPHENYL TRIKETONE, 13, 38
DITHIOSALICYLIC ACID, 12, 76
Di-*p*-tolylethane, 10, 110
Di-*p*-tolylmercury, 14, 86
n-DODECYL ALCOHOL, 10, 62; 13, 108; 14, 87; 15, 24
n-DODECYL BROMIDE, 15, 24; 16, 35
n-Dodecyl cyanide, 16, 35
DURENE, 10, 32; 11, 101; 15, 88
DUROQUINONE, 10, 40
Dyes
  azo, preparation, 16, 12
  capillary test for purity, 16, 16
  spot test, 16, 13

ENANTHIC ACID, 16, 39
EPIBROMOHYDRIN, 16, 31
EPICHLOROHYDRIN, 13, 106; 16, 30
1,4-EPOXYBUTANE, 16, 77
ERUCIC ACID, 10, 44
Esterification, 10, 48, 70, 88; 11, 42; 13, 16, 42; 17, 32
ETHOXYACETIC ACID, 13, 42
Ethyl acetoacetate, 14, 31, 38; 15, 17; 17, 63
ETHYL ACETOSUCCINATE, 14, 38
Ethyl β-acetotricarballylate, 14, 39
Ethyl adipate, 17, 30, 32

Ethyl alcohol, anhydrous, 17, 87
Ethyl *p*-aminobenzoate, 10, 110; 13, 52, 54
Ethyl benzoate, 10, 51
Ethyl benzoylformate, 16, 89
Ethyl benzyl ketone, 16, 49
Ethyl bromide, 11, 98; 12, 86; 15, 88; 16, 86; 17, 48
Ethyl bromomalonate, 11, 36
Ethyl *iso*-butylmalonate, 11, 22
Ethyl *n*-butylmalonate, 10, 109; 11, 21, 22, 78
Ethyl *sec.*-butylmalonate, 11, 22, 76, 77
Ethyl *n*-butyrate, 13, 24
Ethyl carbonate, 11, 98
Ethyl chelidonate, 17, 40
Ethyl chloroformate, 12, 38; 17, 49
Ethyl cinnamate, 12, 36
ETHYL α,β-DIBROMO-β-PHENYLPROPIONATE, 12, 36, 60
Ethyl dihydroxymalonate, 10, 57
Ethylene, 17, 25
Ethylene chlorohydrin, 12, 68; 14, 28, 55
Ethylene cyanohydrin, 15, 88
Ethylene dibromide, 10, 96
ETHYL ETHOXALYLPROPIONATE, 17, 54, 56
ETHYL ETHOXYACETATE, 13, 42
ETHYL ETHYLENETETRACARBOXYLATE, 11, 36; 17, 91
Ethyl *p*-fluorobenzoate, 13, 53
Ethyl formate, 10, 1, 2; 15, 11
  purification, 15, 13
ETHYL FUMARATE, 10, 48; 11, 102
Ethyl iodide, 12, 86; 13, 62
Ethyl laurate, 10, 62
Ethyl maleate, 10, 51
Ethyl malonate, 10, 55, 58; 11, 77; 15, 14; 16, 60; 17, 86
ETHYL METHANETRICARBOXYLATE, 17, 86
ETHYL *N*-METHYLCARBAMATE, 12, 38; 13, 84
Ethyl methyl ketone, 10, 23; 17, 74
Ethyl methyl ketoxime, 11, 59
ETHYL METHYLMALONATE, 17, 56
Ethyl 1-methylthiol-3-phthalimidopropane-3,3-dicarboxylate, 14, 58
Ethyl nitrite, 10, 22, 25
ETHYL *N*-NITROSO-*N*-METHYLCARBAMATE, 13, 84
Ethyl orthoformate, 16, 41
Ethyl oxalate, 10, 51; 11, 40; 16, 33; 17, 40, 54
ETHYL OXOMALONATE, 10, 54, 110; 15, 88; 16, 86
Ethyl pentadecylate, 16, 37
Ethyl pentanehexacarboxylate, 10, 59
Ethyl phenylacetate, 16, 33
ETHYL PHENYLCYANOPYRUVATE, 11, 40
Ethyl β-phenylethyl ketone, 16, 49
ETHYL PHENYLMALONATE, 16, 33
Ethyl phenyloxaloacetate, 16, 33
Ethyl phthalimidomalonate, 14, 58
ETHYL PIMELATE, 11, 42; 17, 91
Ethyl propanetetracarboxylate, 10, 58
Ethyl propionate, 17, 54
Ethyl *iso*-propylmalonate, 11, 20, 21
Ethyl salicylate, 10, 51; 11, 43
Ethyl sebacate, 14, 20
Ethyl sodium phthalimidomalonate, 14, 58
ETHYL *n*-TRIDECYLATE, 16, 35
Explosions, 12, 55; 13, 85; 16, 90

Fermentation, 10, 84
Filtration, inverted, 16, 81
Flavianic acid, 12, 5
Fluoboric acid, 13, 46, 52
Fluorene, 13, 74
FLUOROBENZENE, 13, 46; 15, 89; 16, 86
p-FLUOROBENZOIC ACID, 13, 52; 16, 86
Formaldehyde, 10, 58; 13, 57; 14, 31, 92; 16, 81
Friedel-Crafts reaction, 10, 32; 12, 16, 62, 80; 13, 12, 32; 15, 77
FUMARIC ACID, 10, 50; 11, 46
Furan, 13, 107; 14, 86; 16, 78; 17, 91
2-Furancarboxylic acid, 13, 107, 111
Furfural, 11, 46; 13, 107
Furoic acid, 13, 107, 111; 17, 92
2-Furylcarbinol, 13, 111; 16, 86

Gabriel phthalimide synthesis, 12, 10; 14, 58

GALLACETOPHENONE, **14**, *40*
Gamma acid, **16**, 16
Gattermann-Koch synthesis, **12**, 80
Gelatine, **12**, 4
Glutamic acid, **10**, 111; **13**, 107
d-Glutamic acid, **17**, 92
GLUTARIC ACID, **10**, *58*; **14**, 86, *90*; **17**, 92
Glutaric anhydride, **13**, 13
dl-GLYCERIC ALDEHYDE, **11**, *50*; **14**, 86
dl-GLYCERIC ALDEHYDE ACETAL, **11**, 50, *52*
Glycerol, **14**, 4, 42
GLYCEROL α,γ-DIBROMOHYDRIN, **14**, *42*; **16**, 31
Glycerol α,γ-dichlorohydrin, **16**, 30
Glycine, **10**, 111; **13**, 107; **14**, 86; **15**, 89; **16**, 86
GLYCINE ETHYL ESTER HYDROCHLORIDE, **14**, *46*; **16**, 86; **17**, 92
Grignard reaction
  in *n*-butyl ether, **11**, 84
  with acetaldehyde, **12**, 48
  with butyl *p*-toluenesulfonate, **10**, 4
  with carbon dioxide, **11**, 80
  with dimethyl sulfate, **11**, 66
  with ethyl carbonate, **11**, 98
  with ethyl formate, **15**, 11
  with ethyl orthoformate, **16**, 41
  with water, **11**, 84
Grignard reagent
  from *n*-amyl bromide, **16**, 41
  from benzyl chloride, **10**, 4; **17**, 89
  from bromomesitylene, **11**, 66
  from α-bromonaphthalene, **11**, 80
  from 2-bromopentane, **11**, 84
  from *n*-butyl bromide, **15**, 11
  from ethyl bromide, **11**, 98; **17**, 48
  from *iso*-propyl bromide, **12**, 48
Grignard synthesis
  of an acid, **11**, 80
  of an aldehyde, **16**, 41
  of an ester, **17**, 48
  of a hydrocarbon, **10**, 4; **11**, 66, 84
  of a secondary alcohol, **12**, 48; **15**, **11**
  of a tertiary alcohol, **11**, 98; **17**, 89
Guanidine nitrate, **13**, 107; **17**, 92

unsym.-HEPTACHLOROPROPANE, **17**, *58*
Heptaldehyde, **11**, 54; **14**, 91; **16**, 39
HEPTALDOXIME, **11**, *54*, 58
Heptamethylene glycol, **14**, *22*
HEPTANOL-2, **10**, *60*
Heptanonitrile, **11**, 54
n-HEPTOIC ACID, **16**, *39*
n-Heptyl alcohol, **14**, 87, 91
n-HEPTYLAMINE, **11**, 55, *58*; **17**, 92
n-Heptyl bromide, **15**, *26*; **16**, 60
Hershberg stirrer, **17**, 31
n-HEXADECANE, **15**, *27*; **17**, 92
n-HEXADECYL ALCOHOL, **10**, 64; **15**, *29*
n-HEXADECYL IODIDE, **15**, 27, *29*
n-HEXALDEHYDE, **16**, *41*
Hexamethylbenzene, **10**, 35; **11**, 101
HIPPURIC ACID, **12**, *40*; **13**, 8; **14**, 81
Hoesch reaction, **15**, 70
Hofmann degradation, **16**, 1, 4
HOMOVERATRIC ACID, **15**, *31*; **16**, 87
Hydrazine sulfate, **10**, 111; **13**, 36; **15**, 62; **16**, 18, 51
HYDROBROMIC ACID, **17**, 92
Hydrocarbon, saturated, preparation **11**, 84; **15**, 27
Hydrocinnamic acid, **16**, 49
Hydrofluoric acid, **13**, 46, 52
Hydrofluoric acid burns, **13**, 48
Hydrogenation, **17**, 45
HYDROGEN BROMIDE (anhydrous), **15**, 24, *35*
Hydrogen chloride, **12**, 80; **13**, 43; **16**, 44; **17**, 85
Hydrogen cyanide (anhydrous), **15**, 89
Hydrogen peroxide, **13**, 94; **15**, 31; **16**, 4
Hydrogen sulfide, **16**, 81
Hydrolysis
  of an acetal, **11**, 50; **16**, 42
  of an acetate, **17**, 34
  of an azlactone, **14**, 80; **15**, 31
  of an ester, **17**, 41, 63
  of a dihalide, **12**, 12; **13**, 38, 68
  of a ketimine, **17**, 7
  of a malonic ester, **11**, 20, 76; **14**, 58; **16**, 61
  of a nitrile, **11**, 4, 96; **13**, 95; **16**, 4; **17**, 4
  of a protein, **10**, 100; **12**, 4

Hydrolysis, (*Continued*)
  of a Schiff's base, **12**, 6, 30
  of a sulfonic acid, **14**, 14
  of a sulfonyl chloride, **15**, 55
p-HYDROXYBENZOIC ACID, **14**, *48*
2-HYDROXY-3,5-DIIODOBENZOIC ACID, **14**, *52*
4-Hydroxy-3,5-diiodobenzoic acid, **14**, *53*
β-HYDROXYETHYL METHYL SULFIDE, **14**, 18, *54*
Hydroxylamine hydrochloride, **15**, 85

Identification of sulfonic acid, **16**, 65
Iodination, **11**, 62
  by iodine chloride, **12**, 28; **14**, 52
  by sodium iodide, **17**, 74
  of thiophene, **12**, 44
Iodine, **11**, 62; **12**, 44; **13**, 60; **14**, 12, 53; **15**, 29
Iodine monochloride, **12**, 28, *29*; **14**, *53*
p-IODOANILINE, **11**, *62*
o-Iodophenol, **14**, 87
p-IODOPHENOL, **15**, *39*
IODOTHIOPHENE, **12**, *44*; **16**, 90
ISODURENE, **10**, 37; **11**, *66*
ISONITROSOPROPIOPHENONE, **16**, *44*
ITACONIC ACID, **11**, 29, *70*; **13**, *111*
ITACONIC ANHYDRIDE, **11**, 28, *70*

J acid, **16**, 16

Ketene, **10**, 111; **13**, 107; **15**, 89; **17**, 29, 92
α-Ketoaldehydes, **15**, 67
2-KETOHEXAMETHYLENIMINE, **17**, 7, *60*
Ketone synthesis
  by Friedel-Crafts reaction, **12**, 16,62; **13**, 32, 90; **15**, 77
  by Hoesch reaction, **15**, 70
  by oxidation, **15**, 41; **17**, 43
Ketones, preparation from acids, **16**, 47
α-KETOTETRAHYDRONAPHTHALENE, **15**, *77*
Knoevenagel reaction, **10**, 58

LAURYL ALCOHOL, **10**, *62*; **13**, 108; **14**, 87; **15**, 24
LAURYL BROMIDE, **15**, *24*; **16**, 35
Liebermann-Burchard reaction, **17**, 46

Magnesium, **10**, 4; **11**, 66, 80, 84, 98; **12**, 48; **15**, 11; **16**, 41; **17**, 48, 86, 89
MALONONITRILE, **10**, *66*
Malonylurea, *see* Barbituric acid
l-Menthone, **14**, 87; **17**, 92
Mercuration, **12**, 46, 54
Mercuric chloride, **12**, 54
Mercuric oxide, **12**, 44; **15**, 62
MERCURY DI-β-NAPHTHYL, **12**, *46*
MESACONIC ACID, **11**, *74*
Mesitylene, **11**, 24, 67; **14**, 68, 87; **17**, 92
Mesityl oxide, **15**, 14
dl-METHIONINE, **14**, 58
METHONE, **15**, *14*
METHOXYACETONITRILE, **13**, *56*
Methylamine, **12**, 38
Methylamine hydrochloride, **10**, 112; **15**, 48
Methyl *n*-amyl ketone, **10**, 60; **14**, 87
Methylaniline, **13**, 82
Methylation
  of benzalazine, **16**, 51
  of dibenzoylhydrazine, **16**, 19
  of hydroxyacetonitrile, **13**, 56
  of mesitylene, **11**, 66
  of pyridine, **15**, 41
  of thiourea, **12**, 52
  of vanillin, **13**, 102; **16**, 91
Methyl benzoate, **10**, *51*; **13**, 86; **15**, 32
Methyl benzoyl ketoxime, **16**, *44*
METHYL BENZYL KETONE, **16**, *47*
Methyl chloride, **10**, 32, *36*
Methyl chloroformate, **13**, 100
Methyl cyanide, **15**, 70
Methyleneaminoacetonitrile, **14**, 46
Methylene bromide, **10**, 112; **16**, 87
Methyl ethyl ketone, **10**, 23; **17**, 74
Methyl ethyl ketoxime, **11**, 59
5-METHYLFURFURAL, **14**, *62*
α-Methyl-*d*-glucoside, **10**, 112
METHYL HOMOVERATRATE, **15**, *31*
METHYLHYDRAZINE SULFATE, **16**, *51*

METHYL IODIDE, **13**, *60*
S-METHYLISOTHIOUREA SULFATE, **12**, *52*; **14**, 54
Methyl β-naphthyl ketone, **17**, 65
Methyl nitrite, **16**, 44
METHYL OXALATE, **10**, *70*
3-METHYLPENTANOIC ACID, **11**, *76*
Methyl β-phenylethyl ketone, **16**, *49*
α-METHYL-α-PHENYLHYDRAZINE, **13**, *66*
METHYL *iso*-PROPYL CARBINOL, **12**, *48*; **13**, 108
METHYL *iso*-PROPYL KETONE, **13**, *68*
1-METHYL-2-PYRIDONE, **15**, *41*
1-Methylthiol-3-phthalamidopropane-3,3-dicarboxylic acid, **14**, 59
6-METHYLURACIL, **17**, *63*
Monochloromethyl ether, **14**, 92
Morland salt, **15**, 75
Myristyl alcohol, **10**, 64
Myristyl bromide, **15**, *26*; **16**, 37

Naphthalene, **10**, 14; **16**, 68
β-Naphthalenediazonium chloride, mercuric chloride compound, **12**, 46, 55; **16**, 90
α-NAPHTHOIC ACID, **11**, *80*; **17**, 92
β-NAPHTHOIC ACID, **17**, *65*
α-Naphthol, **17**, 10
β-Naphthol, **11**, 8, 12; **17**, 9
Naphtholsulfonic acids, coupling, **16**, 16
α-NAPHTHOQUINONE, **17**, *68*
β-NAPHTHOQUINONE, **17**, *68*
β-Naphthylamine, **12**, 54
γ-Naphthylbutyric acids, **17**, 97
α-(β-Naphthyl)-ethylamine, **17**, *78*
β-NAPHTHYLMERCURIC CHLORIDE, **12**, *54*; **16**, 90
Nickel, Raney catalyst, **16**, 80
Nicotinic acid, **10**, 112
Nitration
of acetophenone, **10**, 74; **11**, 102; **16**, 87
of acetyl-β-aminonaphthalene, **13**, 72
of barbituric acid, **12**, 58
of fluorene, **13**, 74
of mesitylene, **14**, 68
of phthalimide, **16**, 58
of thiophene, **14**, 76
Nitrile formation, **13**, 56; **15**, 85; **16**, 35
m-NITROACETOPHENONE, **10**, *74*; **11**, 102; **16**, 87; **17**, 92
1-NITRO-2-ACETYLAMINONAPHTHALENE, **13**, 72, 78; **17**, 92
5-Nitro-2-acetylaminonaphthalene, **13**, 73
8-Nitro-2-acetylaminonaphthalene, **13**, 73
p-Nitroaniline, **12**, 28; **14**, 72
NITROBARBITURIC ACID, **12**, *58*, 84
m-Nitrobenzaldehyde, **13**, 28
Nitrobenzene, **11**, 16; **17**, 95
o-NITROBENZENESULFENYL CHLORIDE, **15**, *45*
o-Nitrobenzenesulfonyl chloride, **15**, *55*
m-Nitrobenzoic acid, **16**, 87
p-Nitrobenzoyl chloride, **17**, 93
p-NITROBENZYL BROMIDE, **16**, *54*
o-Nitrochlorobenzene, **14**, 67
m-Nitrochlorobenzene, **10**, 112
p-Nitrochlorobenzene, **14**, 66
o-Nitro-*p*-chlorophenylsulfur chloride, **15**, *46*
o-Nitrodiphenyl ether, **14**, *67*
m-Nitrodiphenyl ether, **14**, 67
p-NITRODIPHENYL ETHER, **14**, 66
2-NITROFLUORENE, **13**, *74*
NITROMESITYLENE, **14**, *68*
1-NITRO-2-NAPHTHOL, **13**, *78*
p-Nitrophenol, **15**, 6
p-NITROPHENYL ISOCYANATE, **14**, *72*
o-NITROPHENYLSULFUR CHLORIDE, **15**, *45*
4-NITROPHTHALIC ACID, **16**, *56*
3-Nitrophthalic anhydride, **15**, 89
4-NITROPHTHALIMIDE, **16**, 56, *58*
Nitrosation
of dimethylamine, **16**, 22
of dimethylaniline, **12**, 30
of ethyl acetoacetate, **15**, 17
of ethyl malonate, **10**, 54
of ethyl *N*-methylcarbamate, **13**, 84
of methylaniline, **13**, 82
of methyl ethyl ketone, **10**, 22
of methylurea, **15**, 48
of propiophenone, **16**, 44
Nitrosodimethylamine, **16**, 22
p-Nitrosodimethylaniline, **12**, 30

N-NITROSOMETHYLANILINE, **13**, 66, *82*
NITROSOMETHYLUREA, **15**, 3, *48*
NITROSOMETHYLURETHANE, **13**, *84*
Nitroso-β-naphthol, **11**, 8, 12, 13; **17**, 13
NITROTHIOPHENE, **14**, *76*
p-Nitrotoluene, **16**, 54
Nitrourea, **10**, 112
Nonamethylene glycol, **14**, *22*
NONANOL-5, **15**, *11*
n-NONOIC ACID, **16**, *60*
NW acid, **16**, 16

Octadecamethylene glycol, **14**, *22*
9,10-OCTADECENOL-1, **15**, *51*
Octadecyl bromide, **15**, *26*
d- and *l*-Octanol-2, **15**, 92
OLEYL ALCOHOL, **15**, *51*
Orange I, **17**, 10
Orange II, **17**, 9
ORTHANILIC ACID, **15**, *55*
OXALIC ACID (anhydrous), **10**, 70, *78*; **11**, 101
Oxidation
by chlorate (+ V_2O_5), **11**, 46; **16**, 73
by dichromate, **12**, 64; **17**, 43, 69
by ferric chloride, **10**, 40; **17**, 68
by ferricyanide, **15**, 41
by hydrogen peroxide, **15**, 31
by hypochlorite, **15**, 9; **17**, 65
by mercuric oxide, **15**, 62
by nitric acid, **13**, 110; **15**, 55; **17**, 96
by permanganate, **10**, 20, 82; **11**, 52; **13**, 1, 4; **16**, 5, 39, 68
by selenium dioxide, **15**, 67; **16**, 87
by sulfuric acid, **10**, 90
Oximation, **10**, 10, 22; **11**, 54

Palladium catalyst for reductions, **16**, *77*
Pancreatin, **10**, 100
Paraformaldehyde, **13**, 56
Paraldehyde, **17**, 18
PELARGONIC ACID, **16**, *60*
Pentadecylic acid, **16**, 37
Pentaerythritol, **10**, 113; **14**, 87; **17**, 73
PENTAERTHRITYL BROMIDE, **17**, *73*
PENTAERTHRITYL IODIDE, **17**, *73*
Pentamethylbenzene, **10**, *34*; **11**, 101
Pentamethylene bromide, **15**, 93; **16**, 87, 91
n-PENTANE, **11**, *84*; **17**, 93
Pentene-2, **10**, 113
PERBENZOIC ACID, **13**, *86*, 111; **14**, 88
estimation of active oxygen, **13**, 89
Phenanthrene, **16**, 63, 66
PHENANTHRENE-2-and-3-SULFONATES, **16**, *63*
Phenol, **13**, 91; **14**, 14, 66
Phenylacetic acid, **12**, 16; **13**, 10; **14**, 88; **16**, 28, 48, 87
PHENYLACETONE, **16**, *47*
Phenylacetyl chloride, **12**, 16
Phenylacetylene, **16**, 87
dl-β-PHENYLANINE, **14**, *80*
PHENYLARSONIC ACID, **15**, *59*
PHENYLBENZOYLDIAZOMETHANE, **15**, *62*
α-PHENYL-β-BENZOYLPROPIONITRILE, **10**, *80*
γ-PHENYLBUTYRIC ACID, **15**, *64*, 77; **17**, *97*
γ-Phenylbutyryl chloride, **15**, *77*
2-PHENYL-4-(3′,4′-DIMETHOXYBENZAL)-OXAZOLONE, **13**, *8*
α-PHENYLETHYLAMINE, **17**, *76*, 80
d-α-PHENYLETHYLAMINE, **17**, *80*
l-α-PHENYLETHYLAMINE, **17**, *80*
d-α-Phenylethylamine-*l*-malate, **17**, 80
l-α-Phenylethylamine-*d*-tartrate, **17**, 81
Phenylethylene, **14**, 89; **16**, 87
α-Phenylethylformamide, **17**, 77
PHENYLGLYOXAL, **15**, *67*; **16**, 87; **17**, 93
Phenylhydrazine, **10**, 113
β-Phenylhydroxylamine, **10**, 113
Phenylmalonic ester, ethyl, **16**, *33*
Phenylmethylglyoxal, **15**, *68*
PHENYLPROPIOLIC ACID, **12**, *60*
Phenyl propionate, **13**, 90, *91*
PHENYL THIENYL KETONE, **12**, *62*
PHLOROACETOPHENONE, **15**, *70*
Phloroglucinol, **14**, 88; **15**, 70
Phosgene, **14**, 72
Phosphorus, **13**, 60; **14**, 42; **15**, 29
Phosphorus oxychloride, **12**, 66; **16**, 9
Phosphorus pentachloride, **12**, 12
Phosphorus tribromide, **13**, 20; **17**, 73

Phosphorus trichloride, **12**, 16
Phosphorus trisulfide, **12**, 72, ***73***
Phthalaldehyde acid, **16**, ***68***; **17**, 93
Phthalic anhydride, **11**, 88; **13**, 10
Phthalide, **16**, ***71***
Phthalimide, **12**, 10; **16**, 58, 71
Phthalimide synthesis, **12**, 10
γ-Phthalimidobutyronitrile, **17**, 4
Phthalyl chlorides, **11**, ***88***
Picryl chloride, **13**, 37
Pimelic acid, **11**, ***43***
Pinacol hydrate, **13**, 111
Pinacolone, **14**, 88
Piperonal, **10**, 82
Piperonylic acid, **10**, ***82***
Pivaloin, **13**, ***26***
Platinum catalyst for reductions, **15**, 89; **16**, 87; **17**, 93, ***98***
Potassium bichromate, **12**, 64
Potassium cyanide, **16**, 35
Potassium ferricyanide, **15**, 41
Potassium hypobromite, **16**, 1
Potassium hypochlorite, **17**, 66
Potassium permanganate, *see* Oxidation
Potassium phthalimide, **17**, 4
Prehnitene, **10**, 37; **11**, 101
Propionaldehyde, **12**, ***64***; **13**, 108
Propionic acid, **13**, 91; **16**, 49
Propionoin, **13**, ***26***
Propionyl chloride, **13**, 91
o-Propiophenol, **13**, ***90***
p-Propiophenol, **13**, ***90***
Propiophenone, **16**, 44
iso-Propyl alcohol, **10**, 88; **14**, 8
n-Propyl alcohol, **12**, 64
n-Propylbenzene, **10**, 113
iso-Propyl bromide, **11**, 92; **12**, 48; **13**, ***21***
n-Propyl bromide, **13**, ***21***; **15**, 72
iso-Propylbromomalonic acid, **11**, ***21***
l-Propylene glycol, **10**, ***84***
n-Propyl iodide, **13**, ***62***
iso-Propyl lactate, **10**, ***88***
n-Propyl phosphate, **16**, ***10***
n-Propyl sulfide, **15**, ***72***
iso-Propyl thiocyanate, **11**, ***92***
Pseudodurene, **10**, 37
Pyridine, **11**, 5; **12**, 20; **15**, 41; **16**, 9
Pyrogallol, **14**, 40
Pyromellitic acid, **10**, ***90***
γ-Pyrone-2,6-dicarboxylic acid, **17**, ***40***
Pyrrole, **10**, 113; **15**, 89
Pyruvic acid, **10**, 114; **15**, 90

Quinizarin, **14**, 88; **15**, 90; **16**, 87
Quinoline, **10**, 114; **16**, 88
Quinone, **16**, ***73***

R acid, **16**, 16
R salt, **16**, 15
Rearrangements, **11**, 28, 74, 89; **13**, 68, 90; **14**, 12; **16**, 1, 4; **17**, 60
Reduction
  by aluminum ethoxide, **15**, 80
  by copper, **12**, 46, 54; **14**, 4
  by dextrose, **17**, 95
  by ethyl alcohol, **13**, 96
  by hydriodic acid, **14**, 80
  by hydrogen and palladium, **16**, 77
  by iron, **11**, 32; **15**, 55
  by reductase of yeast, **10**, 84
  by sodium, **10**, 60, 62; **11**, 42, 58; **13**, 24; **14**, 20; **15**, 51
  by sodium arsenite, **11**, 16
  by sodium bisulfite, **11**, 12
  by sodium hydrosulfite, **11**, 8; **17**, 10, 11
  by stannous chloride, **13**, 28; **14**, 62
  by tin, **12**, 84; **15**, 8
  by zinc, **13**, 66, 74; **15**, 17, 27, 64; **16**, 23, 71; **17**, 97
Reinecke salt, **15**, ***74***
Resolution of a *dl*-amine, **17**, 80
Resorcinol, **10**, 94
β-Resorcylic acid, **10**, ***94***; **17**, 23
Ricinoleic acid, **13**, 4

S acid, **16**, 16
Salicylic acid, **11**, 42; **14**, 48, 52
Schaeffer's acid, **16**, 16
Schaeffer's salt, **16**, 15
Schotten-Baumann acylation, **12**, 41; **16**, 18
Selenious acid, **15**, 67

Selenium dioxide, **15**, 67, ***68***
Silica gel, **17**, 27
Sodium, **13**, 24, 42, 86, 100; **14**, 20; **15**, 14, 51, 72; **16**, 33, 60
Sodium bisulfite, **11**, 12; **16**, 39
Sodium 2-bromoethanesulfonate, **10**, ***96***, 98
Sodium chlorate, **11**, 46; **16**, 73
Sodium cyanide, **13**, 56; **15**, 1
Sodium dimethylglyoximate, **10**, ***24***
Sodium ethylate, **17**, 40, 54
Sodium hydrosulfite, **11**, 8; **17**, 10, 11
Sodium hydroxylamine monosulfonate, **10**, ***23***
Sodium *p*-hydroxyphenylarsonate, **14**, 88
Sodium hypochlorite, **16**, 4
Sodium metabisulfite, **13**, 29
Sodium methylate, **17**, 34
Sodium nitrite, *see* Diazotization, Nitrosation
Sodium 1-nitro-2-naphtholate, **13**, ***78***
Sodium perbenzoate, **13**, ***86***
Sodium succinate, **12**, 72
Sodium sulfide, **12**, 68, 76; **15**, ***72***
Soxhlet extractor, **16**, 69; **17**, 74
Stannous chloride, **17**, 10, 11
Steam distillation, rapid, **17**, 20
Stilbene, **17**, ***90***
Stirrer, Hershberg, **17**, 31
Strecker's synthesis, **11**, 4
Styrene, **14**, 89; **16**, 87
Succinic acid, **12**, 66; **16**, 75
Succinic anhydride, **12**, ***66***; **13**, 12; **15**, ***92***
Succinimide, **15**, 1, ***75***
Sulfanilic acid, **17**, 9
o-Sulfobenzoic anhydride, **17**, 98
Sulfonation, **10**, 6; **11**, 12; **14**, 14; **16**, 63
Sulfonyl chloride, preparation, **10**, 6; **15**, ***55***
Sulfur, as catalyst, **17**, 18
Sulfur chloride, **14**, 36
Sulfur dioxide, **16**, 39

dl-Tartaric acid, **15**, 90
Taurine, **10**, ***98***; **17**, 93
Tetrabromo-1,3-butadiene, **17**, 29
sym.-Tetrabromo-*neo*-pentane, **17**, ***73***
Tetrachloroethylene, **17**, 58
Tetradecamethylene glycol, **14**, ***22***
Tetradecyl bromide, **15**, ***26***; **16**, 37
Tetrahydrofuran, **16**, ***77***; **17**, 84, 93
sym.-Tetraiodo-*neo*-pentane, **17**, ***73***
α-Tetralone, **15**, ***77***; **16**, 91
1,2,3,5-Tetramethylbenzene, **11**, ***66***
1,2,4,5-Tetramethylbenzene, **10**, ***32***
Tetramethylene oxide, **16**, ***77***
Thiobenzophenone, **11**, ***94***
Thiocarbonyl perchloride, **13**, 112
β-Thiodiglycol, **12**, ***68***; **17**, 93
Thionyl chloride, **12**, 20; **13**, 32, 91; **14**, 18; **15**, 77
Thiophene, **12**, 44, 62, ***72***; **14**, 76
Thiophosgene, **13**, 112
Thiosalicylic acid, **12**, ***76***
Thiourea, **12**, 52
Thoria catalyst, **16**, ***47***
Thymoquinone, **17**, 93
Tin, **12**, 84
p-Tolualdehyde, **12**, ***80***; **13**, 109; **15**, 90
o-Toluamide, **11**, 97; **13**, ***94***
Toluene, **12**, 80; **17**, 32, 97
o-Toluic acid, **11**, ***96***
p-Toluic acid, **11**, ***97***
p-Toluidine salts of sulfonic acids, **16**, 65
o-Tolunitrile, **10**, 114; **11**, 96; **13**, 94
p-Tolunitrile, **10**, 114; **11**, 97
α-*p*-Tolylethylamine, **17**, ***78***
Tri-*n*-amyl carbinol, **11**, ***100***
Tribromoaniline, **13**, ***96***
sym.-Tribromobenzene, **13**, ***96***
Tribromoethyl alcohol, **15**, ***84***
Tri-*n*-butyl carbinol, **11**, ***100***
Tricarballylic acid, **10**, 114
Tricarbomethoxymethane, **13**, ***100***
Tricarbethoxymethane, **17**, ***86***
Trichloroaldol, **15**, 83
Trichloroethyl alcohol, **15**, ***80***
Tridecamethylene glycol, **14**, ***22***
Tridecylic acid, **16**, 35
Tridecylic nitrile, **16**, 35
Triethyl carbinol, **11**, ***98***; **13**, 109
Tri-*n*-heptyl carbinol, **11**, ***100***
2,4,6-Trihydroxyacetophenone, **15**, ***70***
Trimethylacetic acid, **13**, 109

Trimethylene chlorohydrin, **17**, 96
Trimethylethylene dibromide, **13**, ***68***
1,3,5-Trinitrobenzene, **13**, 109; **14**, 89; **16**, 88
2,4,6-Trinitrophenylhydrazine, **13**, ***37***
TRIPHENYLETHYLENE, **17**, ***89***
sym.-TRITHIANE, **16**, ***81***
TRITHIOFORMALDEHYDE, **16**, ***81***
Trypan blue, **16**, 15
l-TRYPTOPHANE, **10**, ***100***
l-Tyrosine, **10**, 100, ***102***

Undecamethylene glycol, **14**, ***22***
Undecylenyl alcohol, **10**, ***63***
URAMIL, **12**, ***84***
β-URAMINOCROTONIC acid, **17**, 63
Urea, **12**, 34; **17**, 63
Uric acid, **13**, 1

Vanadium pentoxide, **11**, 46, ***47***; **14**, 90; **16**, 73
Vanillin, **13**, 102; **16**, 91
VERATRIC ALDEHYDE, **13**, 8, ***102***; **15**, 85; **16**, 88, ***91***
Veratric amide, **16**, ***4***, 92
VERATRONITRILE, **15**, ***85***; **16**, 4, 92
γ-Veratrylbutyric acid, **17**, ***97***
Vigreux column, **12**, 86

α-*p*-Xenylethylamine, **17**, ***78***
Xylene, **10**, 32

Yeast, **10**, 84

Zinc-copper couple, **12**, ***87***
Zinc dust, **12**, 77; **13**, 66, 75; **15**, 17, 27; **16**, 23, 71
amalgamated, **15**, 65

ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS

ADVISORY BOARD

ROGER ADAMS
H. T. CLARKE
J. B. CONANT
HENRY GILMAN
C. S. MARVEL
F. C. WHITMORE

EDITORIAL BOARD

L. F. FIESER, *Editor-in-Chief*

W. H. CAROTHERS
R. C. FUSON
JOHN R. JOHNSON
CARL R. NOLLER
W. W. HARTMAN

C. F. H. ALLEN, *Secretary to the Board*
McGill University, Montreal, Canada

CONTRIBUTORS

Other than the members of the Board

HOMER ADKINS	E. B. HERSHBERG	F. A. LONG	J. R. RUHOFF
GÉZA BRAUN	R. M. HIXON	HAKON LUND	R. B. SANDIN
W. F. BRUCE	H. L. HOLMES	E. L. MARTIN	F. E. SCHIEBLEY
G. H. COLEMAN	G. E. HONEYWELL	S. M. MCELVAIN	H. B. SCHURINK
R. F. B. COX	J. W. HOWARD	R. A. MCKEE	P. R. SHILDNECK
C. C. DEWITT	E. H. HUNTRESS	M. S. NEWMAN	DONALD STARR
J. J. DONLEAVY	A. W. INGERSOLL	N. OPOLONICK	AXEL VOIGT
J. C. ECK	M. A. KISE	P. S. PINKNEY	WALTER ZARTMAN
M. W. FARLOW	N. A. LANGE	J. O. RALLS	F. ZWILGMEYER
HANS FISCHER		E. R. RIEGEL	

VOL. XVII

NEW YORK
JOHN WILEY & SONS, INC.
LONDON: CHAPMAN & HALL, LIMITED
1937

Copyright, 1937
BY
ROGER ADAMS

All Rights Reserved

This book or any part thereof must not be reproduced in any form without the written permission of the publisher.

PRINTED IN U. S. A.

PRESS OF
BRAUNWORTH & CO., INC.
BUILDERS OF BOOKS
BRIDGEPORT, CONN

TABLE OF CONTENTS

		PAGE
I.	Aconitic Acid	1
II.	γ-Aminobutyric Acid	4
III.	ε-Aminocaproic Acid	7
IV.	1,2-Aminonaphthol Hydrochloride and 1,4-Aminonaphthol Hydrochloride	9
V.	Benzoylene Urea	16
VI.	Bromal	18
VII.	*p*-Bromobenzaldehyde	20
VIII.	4-Bromoresorcinol	23
IX.	1,3-Butadiene	25
X.	2-Carbethoxycyclopentanone	30
XI.	Cellobiose	34
XII.	α-Cellobiose Octaacetate	36
XIII.	Chelidonic Acid	40
XIV.	Cholestanone	43
XV.	Dihydrocholesterol	45
XVI.	2,4-Dimethyl-5-carbethoxypyrrole	48
XVII.	β, β-Diphenylpropiophenone	51
XVIII.	Ethyl Ethoxalylpropionate	54
XIX.	Ethyl Methylmalonate	56
XX.	*unsym.*-Heptachloropropane	58
XXI.	2-Ketohexamethylenimine	60
XXII.	6-Methyluracil	63
XXIII.	β-Naphthoic Acid	65
XXIV.	β-Naphthoquinone and α-Naphthoquinone	68
XXV.	Pentaerythrityl Bromide and Iodide	73
XXVI.	α-Phenylethylamine	76
XXVII.	*d*- and *l*-α-Phenylethylamine	80
XXVIII.	Tetramethylene Chlorohydrin	84
XXIX.	Tricarbethoxymethane	86
XXX.	Triphenylethylene	89
	Appendix	
	Later References to Preparations in Preceding Volumes	91
	Additions and Corrections for Preceding Volumes	95
	Subject Index	99